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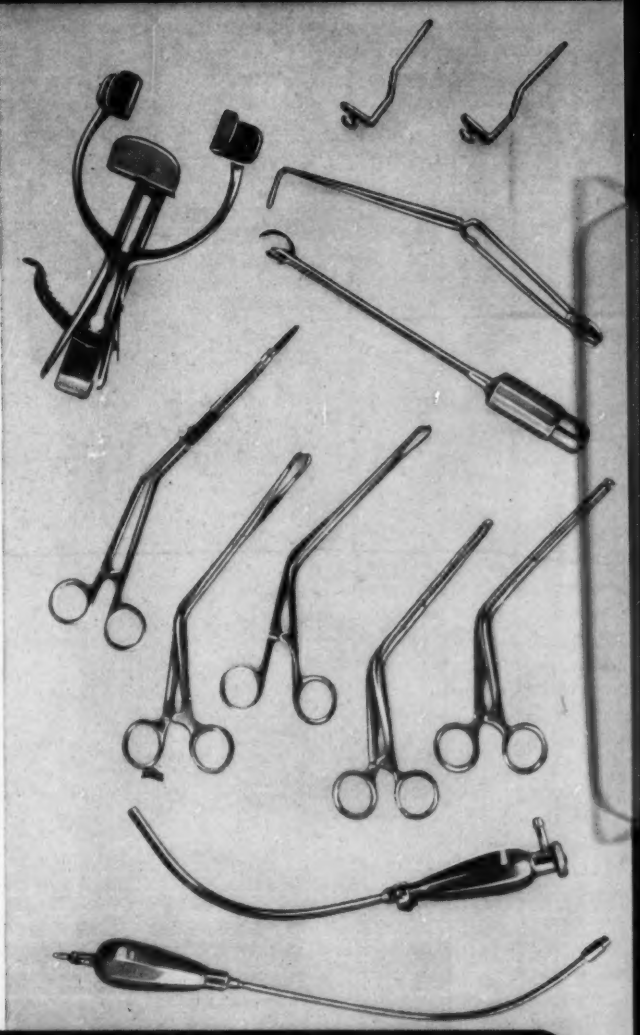

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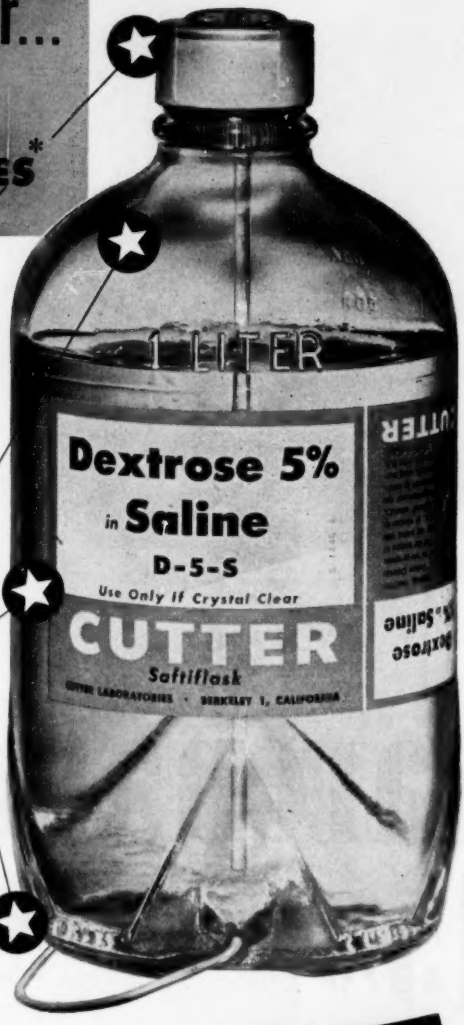

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A STUDY OF VAGOTOMY

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AND
PETER DINEEN, M.D.
NEW YORK

SINCE the report by Dragstedt [1] of 2 patients on whom he performed transthoracic section of the vagus nerves for duodenal ulcer, much interest and investigation have centered on the role of the vagus nerves in gastrointestinal physiology and on their relation to peptic ulcer.

The earliest recorded experiments on the vagus nerves and their effect on the gastrointestinal tract were made in 1814 by Brodie,[2] who observed changes in gastric secretion following division of the vagus nerves in the cervical region in dogs. Hartzell,[3] in his review published in 1929, traced the progress in the understanding of vagus nerve function to the time of Brodie's publication. In 1910 Pavlov [4] demonstrated that intact vagus innervation was necessary for the psychic or cephalic phase of gastric secretion and, through these studies, stimulated the investigation of gastrointestinal physiology.

Vagus section in gastrointestinal surgery was apparently first undertaken by Exner [5] in 1911. He divided the anterior or left vagus nerve in the treatment of gastric tabetic crises and reported on 14 patients subjected to this operation. Dilation, atony and pylorospasm were noted to occur, and in the later cases in his series he added gastrojejunostomy or gastrostomy.

From the Department of Surgery of the New York Hospital and Cornell Medical Center.

1. Dragstedt, L. R., and Owens, F. M., Jr: Supra-Diaphragmatic Section of the Vagus Nerves in Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152, 1943.

2. Brodie, B., cited by Hartzell.

3. Hartzell, J. B.: The Effect of Section of the Vagus Nerves on Gastric Acidity, Am. J. Physiol. **91**:162, 1929.

4. Pavlov, I. P.: The Work of the Digestive Glands, (translated by W. H. Thompson), C. Griffin & Company, London, 1910.

5. Exner, A.: Ein neues Operationsverfahren bei tabischen Crises gastriques, Deutsch. Ztsch. f. Chir. **111**:576, 1911.

From 1920 to 1930 several authors [6] reported methods of vagotomy and their clinical applications; however, the results were questionable or unfavorable, and usually the operations described failed to interrupt all the vagus fibers.

PHYSIOLOGY OF THE VAGUS NERVES

The vagus nerve is concerned with the secretory function of the stomach as well as with the motor functions of the stomach and the small intestine. There is obviously no point in discussing the function of the vagal innervation of the biliary tract, pancreas and other viscera to which the vagus nerve sends fibers.

Pavlov [4] demonstrated in the dog that interruption of the vagus nerves eliminated the cephalic phase of gastric secretion and in addition that the secretion of gastric juice was intermittent. Hartzell [3] extended the experiments of Pavlov and showed that in dogs in which the vagi were sectioned in the thorax there was a marked reduction of both the free and the total acidity and that in plotting the acid secretory response the highest postoperative curve was lower than the lowest preoperative curve. Carlson [7] then showed that in man gastric secretion is continuous even without psychic stimuli or food, containing both pepsin and hydrochloric acid. The normal rate of secretion in the fasting stomach in man is reported variously to lie between 30 to 60 and 15 to 117 cc. per hour, and the total volume is estimated at 2 to 3 liters per day.[8]

In patients with ulcers Winkelstein [9] noted an increased night secretion with continuous high acid content, although the response to histamine was normal in some patients. Dragstedt [10] recorded the night secretion in a control group of patients to be from 261 to 385 cc. for the twelve hour period and an average of 820 cc. in a group of

6. (*a*) Bircher, E.: Die Resektion von Aesten der N. vagus zur Behandlung gastrischer Affektionen, Schweiz. med. Wchnschr. **50**:519, 1920. (*b*) Latarjet, A.: Resection des nerfs de l'estomac, Bull. Acad. de med., Paris **87**:681, 1922. (*c*) Schiassi, B.: The Role of the Pyloro-Duodenal Nerve Supply in the Surgery of Duodenal Ulcer, Ann. Surg. **81**:939, 1925.

7. Carlson, A. J.: Secretion of Gastric Juice in Health and Disease, Physiol. Rev. **3**:1, 1923.

8. Schiffrin, M. J., and Ivy, A. C.: Physiology of Gastric Secretion, Arch. Surg. **44**:399 (March) 1942.

9. Winkelstein, A.: Studies in Gastric Secretion, Am. J. Surg. **15**:523, 1932; One Hundred and Sixty-Nine Studies in Gastric Secretion During the Night, Am. J. Digest. Dis. **1**:778, 1935; The Medical Treatment of Peptic Ulcer Refractory to Sippy Treatment, Surgery **17**:699, 1945.

10. Thorton, T. F.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of Vagus Nerves in Patients with Peptic Ulcer, Proc. Soc. Exper. Biol. & Med. **59**:140, 1945.

patients with ulcers. After vagotomy the patients with ulcers had an average night secretion of 415 cc.

The secretion of gastric juice, high in both pepsin and acid content, is produced by stimulation of the vagus nerves.[11] The sham meal as a test for intact vagus innervation of the stomach has been largely superseded by the insulin test, in which gastric secretion is stimulated by hypoglycemia.[12] It has been demonstrated that complete section of the vagus nerves abolishes the secretion of gastric juice produced by a sham meal or insulin hypoglycemia.[13] After an initial depression the operation has little or no effect on the response to histamine or caffeine.[10]

Vanzant [14] repeated the experiments of Hartzell and described an initial reduction of gastric secretion and a varying effect on motility. In most cases the secretory activity, as judged by a test meal, was found to increase gradually but it did not reach the preoperative level. Vanzant concluded that the reduction in secretion was due not simply to a loss of the psychic phase of secretion but to a reduced reactivity of the secretory mechanism itself. She also stated that the restoration of secretion was not the result of regeneration of the vagus nerves and was not due to influences coming over the splanchnic nerves. The motility was also found to return to normal after a variable length of time.

Sensations of pressure, heat and cold, pain and nausea are not interrupted by division of the vagus supply to the stomach.[15] Gastric mucosal pallor and hypomotility have been observed in the human being after vagotomy, but gastric hyperemia after ingestion of food is not altered.[16] Patients who have been relieved of pain caused by ulcer by means of section of the vagus nerve still experience pain with the introduction of acid into the stomach.[15]

The occurrence of hypomotility and delayed emptying time in man following vagotomy is well known. The effect of vagus section on gastric motility in the experimental animal has been less uniform.

11. Alley, A.: The Secretory Activity of the Gastric Mucosa in the Region of the Lesser Curvature, Tr. Roy. Soc. Canada **27**:71, 1933.

12. Jeremin, E. E.; Hollander, F., and Weinstein, V. A.: A Comparison of Insulin and Food as Stimuli for the Differentiation of Vagal and Non-Vagal Pouches, Gastroenterology **1**:500, 1943.

13. Hollander, F.: Insulin Test for Presence of Intact Nerve Fibers, Gastroenterology **7**:607, 1946.

14. Vanzant, F. R.: The Late Restoration of Gastric Acidity after Thoracic Vagotomy in the Dog, Gastroenterology **8**:768, 1947.

15. Dragstedt, L. R.; Woodward, E. R.; Harper, P. V., and Storer, E. H.: Mechanism of the Relief of Ulcer Distress by Gastric Vagotomy, Gastroenterology **10**:200, 1948.

16. Wolf, S., and Andrus, W. DeW.: The Effect of Vagotomy on Gastric Function, Gastroenterology **8**:429, 1947.

McCrea and his associates [17] found in experiments on dogs that the motility was only slightly decreased and that the disturbance in emptying time was minimal. They stated that the pylorus became patulous and attributed the increased emptying time to this.

Recently Postlethwait and Grimson [18] concluded from experimental and clinical material that the effect of vagotomy in the experimental animals and in man differs. Hypermotility followed vagotomy in 26 rabbits. In dogs the complete emptying time was decreased, and this was associated with an increased resting intragastric pressure and an irregular motility pattern. At autopsies performed two months after operation the stomachs of the dogs were found to be markedly distended. Grimson [19] showed that the amplitude of gastric contractions in patients was decreased and that the average resting intragastric pressure was somewhat increased after section of the vagus nerves. Hypomotility persisted as long as two and one-half years after operation.

Discrepancies have been noted in the application of vagotomy to experimental ulcers. Ulcers have been produced in animals in several ways: by the production of bile and pancreatic fistulas,[20] duodenectomy,[21] isolated stomach preparation,[22] "experimental Meckel's diverticulum," [23] intramuscular injection of histamine in beeswax [24] and other methods. Ophuls,[25] Beaver and Mann,[26] and Greggio [27] were

17. McCrea, E. D.; McSwiney, B. A., and Stopford, J. S. B.: Effect on the Stomach of Section of the Vagi, Quart. J. Exper. Physiol. **16**:195, 1926.

18. Postlethwait, R. W.; Hill, H. V., Jr.; Chittum, J. R., and Grimson, K. S.: Effect of Vagotomy and of Drugs on Gastric Motility, Ann. Surg. **128**:184, 1948.

19. Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. W., and Rundles, R. W.: Transthoracic Vagotomy, J. A. M. A. **134**:925 (July 12) 1947.

20. Berg., B. N.: Peptic Ulcer, Arch. Surg. **28**:1057 (June) 1934. Kapsinow, R.: The Experimental Production of Duodenal Ulcer by Exclusion of Bile for the Intestine, Ann. Surg. **83**:614, 1926.

21. Bickel, A.: Beobachtungen an Hunden mit extirpierten Duodenum, Klin. Wchnschr. **46**:1201, 1909. Grey, E. G.: Duodenectomy: Its Effect upon the Life of an Animal, Surg., Gynec. & Obst. **28**:36, 1919. Mann, F. C., and Kawamura, K.: Duodenectomy, Ann. Surg. **75**:208, 1922.

22. Dragstedt, L. R.: Some Physiological Principles Involved in the Surgical Treatment of Gastric and Duodenal Ulcer, Ann. Surg. **102**:563, 1935.

23. Matthews, W. B., and Dragstedt, L. R.: The Etiology of Gastric and Duodenal Ulcer, Surg. Gynec. & Obst. **55**:265, 1932.

24. Hay, L. J.; Varco, R. L.; Code, C. F., and Wangensteen, O. H.: The Experimental Production of Gastric and Duodenal Ulcer in Laboratory Animals by the Intra-Muscular Injection of Histamine in Beeswax, Surg., Gynec. & Obst. **75**:170, 1942.

25. Ophuls, W.: Gastric Ulcers in Rabbits Following Resection of the Pneumogastric Nerves Below the Diaphragm, J. Exper. Med. **8**:181, 1906.

26. Mann, F. C., and Beaver, M. G.: The Production of Peptic Ulcer after Section of the Gastric Nerve, Ann. Surg. **94**:1116, 1931.

27. Greggio, E.: Des ulceres gastroduodenaux, Arch. de. med. exper. et d'anat. path. **27**:533, 1916.

able to produce gastroduodenal ulceration in rabbits and dogs by bilateral vagotomy. Ferguson described mucosal erosions in 2 of 10 monkeys subjected to this operation.[28] Grimson [18] found that in one fifth of the rabbits that he studied gastric ulcers developed, but he failed to find evidence of ulcerations in dogs. The Mann-Williamson operation was described in 1923.[29] It has become a standard method for the production of experimental peptic ulcer and is frequently used to produce ulcer in order to evaluate experimental methods of healing or of protecting the animals from ulcer formation. Though vagotomy has been found to protect the isolated stomach preparation,[22] it fails to prevent the formation of the histamine-provoked ulcer [30] or of ulcer in the Mann-Williamson preparation.[31] Dragstedt [32] has recently commented on these findings by pointing out the difference between the ulcer produced in the Mann-Williamson operation and the stoma ulcer in man. With the former, the duodenal secretions are completely diverted into the lower intestine, which is not the case with the usual gastrojejunostomy. In addition he cited 2 patients on whom operations of the Roux Y type had been performed and in whom marginal ulcers developed. Vagotomy failed to relieve their recurrent ulcers.

Roentgenographic demonstration of atonicity and irregular and infrequent gastric contractions has been described by many and is a usual finding in patients after vagotomy. It appears to be less pronounced when the operation is supplemented by gastrojejunostomy or pyloroplasty.[33] Ritvo and Schauffer [34] found a return toward normal within six months to a year as demonstrated by barium studies, although complete return to normal was not found in any of their cases as long as fourteen months after section of the vagus nerve.

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28. Ferguson, J. H.: Effects of Vagotomy on the Gastric Functions of Monkeys, Surg., Gynec. & Obst. **62**:689, 1936.

29. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409, 1923.

30. Harkins, H. N.; Hooker, D. H.; Alford, T. C.; Callender, J.; Elliott, S. R.; Kearns, W.; Mitchener, J., and Cooley, D.: Symposium on Vagotomy for Peptic Ulcer: I. Experimental Observations, Bull. Johns Hopkins Hosp. **81**:79, 1947.

31. Oliver, J. V.: Effect of Vagotomy on the Development of the Mann-Williamson Ulcer in the Dog, Arch. Surg. **55**:180 (Aug.) 1947.

32. Dragstedt, L. R.: Vagotomy and the Mann-Williamson Ulcer, editorial, Surg., Gynec. & Obst. **87**:749, 1948.

33. Johns, T. N. P., and Grose, W. E.: Symposium on Vagotomy for Peptic Ulcer: II. Early Surgical Results in Forty-Three Cases, Bull. Johns Hopkins Hosp. **81**:92, 1947.

34. Ritvo, M., and Schauffer, I. A.: Roentgenographic Studies of the Gastro-Intestinal Tract Following Section of Vagus Nerves for Peptic Ulcer, New England J. Med. **238**:496, 1948.

The role of the vagus in the function of the small intestine is somewhat more obscure. Three types of motor activity have been described by Cannon,[35] consisting of segmentation, peristaltic waves and pendulum movement. Segmentation refers to the simultaneous division of intestinal contents into a series of fairly uniform segments and has been described in both the experimental animal and man. Peristaltic movement is of two types—the slowly advancing wave and the rapid peristaltic rush. Segmentation is apparently concerned with the mixing of the intestinal contents, whereas peristalsis is a means of propelling the contents of the bowel along the intestinal tract. Pendulum movement is "characterized by a gentle swaying of the coils, and is accompanied by rhythmical contractions."

The application of nicotine locally abolishes the peristaltic waves of the small intestine but does not obliterate segmentation.[36] This indicates that peristalsis is governed by extrinsic innervation and that segmentation is mediated through the intrinsic plexus of Meissner and Auerbach.

The increase in peristalsis in the small intestine associated with excitement [37] also suggests influence of the central nervous system. Whether the vagus or the sympathetic nervous system mediates these changes has not been demonstrated to our knowledge.

The vagus nerve is reported to carry both motor and inhibitory fibers to the small intestine, with a predominance of the former.[38] Stimulation of the vagus nerve results in an increase in the tonus of the small bowel and an increase in rhythmic contractions.[38] Alvarez [39] stated that after section of the vagi there is "less tendency for rush waves to start off down the bowel and it has been harder to make them go." Others [34] have stated that there is no change in the size of the small bowel after vagotomy but that the motility is reduced. The latter finding is credited to delayed emptying of the stomach.

Varying effects of vagus stimulation on the function of the large intestine have been reported. Bayliss and Starling [36] were unable to demonstrate any effect on the colon of the dog, and Ivy [40] stated that the electrical stimulation of the vagus is ineffective in producing a response in the colon of this animal. He found weak and inconsistent

35. Cannon, W. B.: The Mechanical Factors of Digestion, London, Edward Arnold & Company, 1911.

36. Bayliss, and Starling: J. Physiol. **26**:114, 1900; cited by Cannon.

37. Weeks, D. M.: Observations of Small and Large Bowel Motility in Man, Gastroenterology **6**:185, 1946.

38. Starling: Ergebn. d. Physiol. **1**:460, 1902; cited by Cannon.

39. Alvarez, W. C.: The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, Inc., 1929.

40. Wells, J. A.; Mercer, T. H.; Grey, J. S., and Ivy, A. C.: Motor Innervation of the Colon, Am. J. Physiol. **138**:83, 1942.

responses in the cecum of the pig and the monkey. Meltzer and Auer [41] were able to cause strong contractions in the cecum of rabbits by vagal stimulation.

The production of gastric atony, decreased motility and increased emptying time results in man in the symptoms of fulness, nausea, anorexia and belching. Johns and Grose [33] reported that 67 per cent of their patients suffered from symptoms of disturbed gastrointestinal physiology after vagus section. Gastric retention may be serious enough to require secondary operation. Grimson [19] found gastroenterostomy necessary in 5 of 57 cases, Harkins and Hooker in 1 of 26 cases and Weinberg and his associates in 4 of their 60 cases.

Machella, Hodges and Lorber [42] found that gastric motility could be restored after vagotomy by the use of urethane of beta methylcholine chloride (urecholine®), and this has been confirmed by Postlethwait.[18] Carbaminoylcholine (doryl®) has also been found to be effective in restoring gastric motility.[18] These drugs are stable choline derivatives and are strong stimulants of gastric secretion as well as of motility.[43] Methacholine chloride (mecholyl chloride®) is considerably less effective.[18]

The occurrence of diarrhea following vagotomy may be more troublesome in some cases than the symptoms of gastric atony. Thirty-eight per cent of Miller's patients [44] had diarrhea postoperatively, and Grimson [19] noted the symptom in 12 of 57 patients, or 21 per cent. As in the case of gastric retention, the diarrhea lasts a varying length of time and gradually disappears. The cause of it has not been established. Dragstedt [45] postulated that anacidity following vagotomy renders the patients more susceptible to diarrhea of bacterial origin. Moore [46] suggested that it is an intestinal manifestation of intermittent gastric emptying interspersed with periods of gastric stasis. Walters [47] felt

41. Meltzer and Auer: Proc. Soc. Exper. Biol. & Med. **4**:39, 1907; cited by Cannon.

42. Machella, T. E.; Hodges, H. H., and Lorber, S. H.: The Restoration of Gastric Motility by Urethane of B-Methylcholine after Section of the Vagus Nerves for Peptic Ulcer, Gastroenterology **8**:36, 1947.

43. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.

44. Miller, E. M., and Olwin, J. H.: Results of Resection of the Vagus Nerve for Chronic Peptic Ulcer, Arch. Surg. **57**:353 (Sept.) 1948.

45. Dragstedt, L. R., in discussion on Colp, R.; Klingenstein, P.; Druckerman, L. J., and Weinstein, V. A.: A Comparative Study of Subtotal Gastrectomy With and Without Vagotomy, Ann. Surg. **128**:476, 1948.

46. Moore, F. D.: Vagus Resection for Ulcer: An Interim Evaluation, Ann. Surg. **126**:664, 1947.

47. Walters, W., in discussion on Dragstedt, Harper, Tovee and Woodward,[40] p. 707.

that jejunitis, which he found in some cases with persistent symptoms after vagus section, might contribute to the diarrhea. Dragstedt [45] stated that he did not believe that the diarrhea is caused by release of vagal innervation of the lower part of the intestinal tract for it does not follow gastric resection, which, according to him, usually removes the vagal innervation below the level of the stomach.

ANATOMIC DISTRIBUTION

The anatomic location and distribution of the vagus nerves are important in a consideration of the feasibility of complete surgical division of these structures. With the recent interest in vagotomy, several anatomic studies have been published, for descriptions in the standard textbooks have been found inadequate.

More than two decades ago McCrea [48] studied the paraesophageal distribution of the vagus nerve and described the anterior and posterior divisions which supply the stomach. He noted the hepatic branch and demonstrated that it innervated the pyloric sphincter. McCrae stated that there was a decided similarity in the distribution of the vagus in the dog and in man.

Dragstedt and his co-workers,[49] who examined 60 cadavers in reference to the distribution of the vagus nerve after vagotomy, described a single anterior and posterior division at the level of the lower part of the esophagus in 81 per cent.

Doubilet, Shafiroff and Mulholland [50] studied the anatomy of the vagus nerve below the pulmonary plexus in 32 cadavers and found considerable variation in the number of fibers passing through the esophageal hiatus. In only 20 cases was there a single anterior and a single posterior trunk. In addition they found the hepatic branch arising from the posterior trunk in 3 cases and from both trunks in 3 other cases.

Walters and his associates [51] dissected 100 cadavers, including those of 11 children, and discovered the distribution of the vagus to be about 90 per cent uniform. In the remaining 10 per cent considerable variation was described, and in some of these numerous branches were found that failed to form common trunks on one or both sides of the esophagus.

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48. McCrea, E. D.: Abdominal Distribution of the Vagus, J. Anat. **59**:18, 1924.

49. Dragstedt, L. R.; Fournier, H. J.; Woodward, E. R.; Tovee, E. B., and Harper, P. V.: Transabdominal Gastric Vagotomy, Surg., Gynec. & Obst. **85**:461, 1947.

50. Doubilet, H.; Shafiroff, B. G. P., and Mulholland, J. A.: The Anatomy of the Peri-Esophageal Vagi, Ann. Surg. **127**:128, 1948.

51. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Consideration of Gastric Neurectomy, J. A. M. A. **133**:459 (Feb. 15) 1947.

Miller and Davis,[52] after 13 dissections, found less uniformity and described "normal" anterior and posterior divisions in only 3. Jackson [53] has recently proposed an interesting variation in the technic of vagotomy based on anatomic studies. He suggested section of the posterior trunk in a manner that preserves the celiac division. Having found in his dissections that multiple trunks are more often anterior in the subdiaphragmatic portion of the esophagus, he urged that the operative approach be made from this aspect.

From the anatomic studies published it seems reasonable to conclude that in the majority of cases, probably at least 80 per cent, more or less discrete anterior and posterior trunks will be found. In the remaining instances considerable variation of the distribution of the vagus nerves may be expected, and in some of these the multiplicity of fibers may present a difficult problem in the accomplishment of complete division of the vagus supply to the stomach. Accordingly, one might expect a higher incidence of failure in the latter group.

EXPERIMENTAL DATA

Experiments on motility have been performed in 13 dogs. Studies of gastric motility were made in 12 and records of motility in the small intestine in 8. Tracings were made with an ink-writing air tambour connected to a water manometer. The gastric balloon was inflated with 150 cc. of air, and the balloon for the small intestine contained 20 cc. of air. With the exception of one gastric tracing, all experiments were made with the animals anesthetized with intravenous injections of pentobarbital sodium. Studies of both types of motility were made at intervals from the immediate postoperative period up to five weeks after vagotomy.

Vagotomy was performed by a transthoracic approach except in one instance, in which a transabdominal section was made. Autopsies were carried out in all cases, and complete vagotomy had been accomplished in all dogs except 1.

In the studies of motility in the small intestine, two types of approaches were employed for insertion of the balloon. In 4 dogs the balloon was inserted through an isoperistaltic fistula produced by means of an end to side duodenoduodenostomy. In the others the balloon was introduced through an enterotomy opening at laparotomy, which was closed at the completion of the procedure. The latter method gave equally satisfactory results and was tolerated better. The method has several disadvantages because of the changes associated with laparotomy

52. Miller, E. M., and Davis, C. B., Jr.: An Anatomic Study of the Vagus Nerves, J. A. M. A. **133**:461 (Feb. 15) 1947.

53. Jackson, R. G.: Anatomic Study of the Vagus Nerves, Arch. Surg. **57**:333 (Sept.) 1948.

and with exposure and manipulation of the bowel. However, the bowel was handled as carefully as possible, and the portion studied was not removed from the abdomen. The balloon was placed in the upper region of the jejunum approximately 25 to 30 cm. from the operative site during the recording. Observations were carried out over two to four hour periods.

Considerable variation in motility was found after vagotomy. The tracings of gastric motor activity showed a decrease in amplitude and frequency of contractions, as illustrated in figure 1. There was only minimal activity five weeks after vagus section. These changes persisted

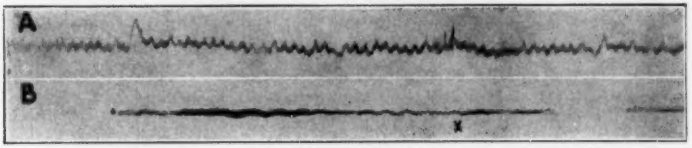

Fig. 1.—Kymographic record of gastric motility in dog 806. *A*, tracing obtained before vagus section. *B*, record five weeks after transthoracic vagotomy; 0.5 mg. of neostigmine bromide was given intramuscularly at *x*. (Each of the records is twenty-five minutes in duration. The kymograph was run at a similar speed in the tracings shown.)

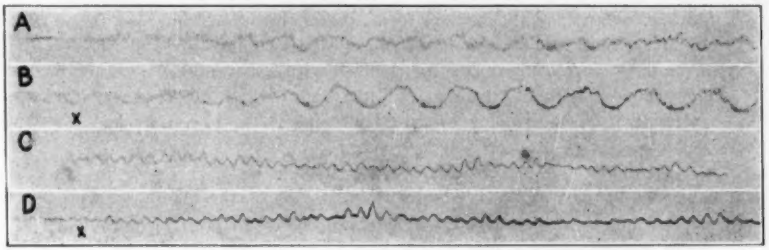

Fig. 2.—Record of motility of the small intestine (upper part of the jejunum) in dog 841. *A*, control record. *B*, control record; 0.5 mg. of neostigmine bromide given intramuscularly at *x*. Note accentuation of regular peristaltic activity. *C*, motility tracing taken thirty minutes after transthoracic section of vagus nerves. *D*, continuation of *C*, 0.455 mg. of neostigmine bromide given intramuscularly at *x*.

throughout the period in which the animals were studied although the degree varied somewhat in different animals. No studies were made of emptying time, nor were measurements made of the intragastric pressure. At autopsy the stomachs were found to be somewhat distended and contained undigested food, but there was not the pronounced distention described by Postlethwait.[18] Ulceration was not found in any case.

Records of motility of the small bowel have been difficult to interpret. Before vagotomy there were fairly regular contractions of twenty to twenty-five seconds interspersed with shorter contractions of three to five seconds. After section of the vagi there was a definite change in the general configuration and the prolonged contractions were usually absent or appeared infrequently. There was considerable variation in the pattern throughout the period of observation. The contractions of briefer duration occurred with smaller amplitude in some cases but not in others after vagotomy. Figure 2 demonstrates the two types of waves before vagotomy and shows the absence of the prolonged contractions after operation. These contractions were not always as well demonstrated as in the case presented.

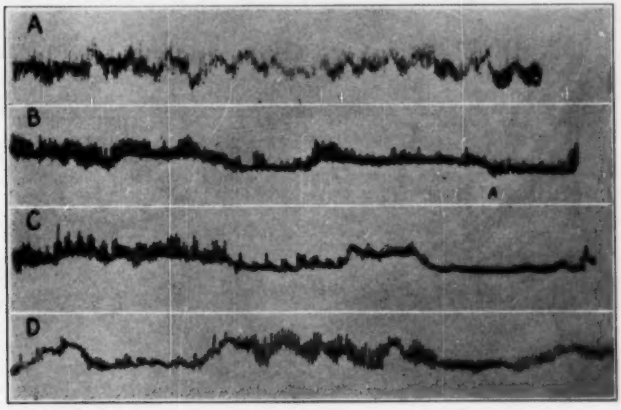

Fig. 3.—Motility of small intestine in dog 757. *A*, control record. Fairly regular contractions are somewhat obscured by vigorous respiratory activity. *B*, record obtained three days after transthoracic vagotomy; 0.5 mg. of neostigmine bromide given intramuscularly at *A*. *C*, continuation of tracing *B* showing same irregular pattern without response to neostigmine. *D*, tracing obtained one week after vagotomy. The record begins fifteen minutes after intramuscular injection of 5 mg. of urecoline.® The control period record was similar to *B* and *C*.

In the study of the effect of drugs on motility of the small intestine neostigmine and urecholine® were used. Before division of the vagus nerve, neostigmine produced an exaggeration of the existing pattern while after section it failed to stimulate a similar response (fig. 2). Urecholine® uniformly increased the motor activity of the small bowel after vagotomy, as illustrated in figure 3.

Studies of gastric motility were performed on 6 patients. Prior to operation, the patients were uniformly found to have active gastric contractions, as seen in figure 4. After section of the vagus nerves

the activity was absent or markedly diminished, as shown in figures 4 and 5. Neither intramuscular injection of neostigmine nor insulin hypoglycemia produced an increase in gastric motor activity after the vagi were divided. Figure 5 demonstrates the marked response to subcutaneous administration of carbaminoylcholine in a patient who had undergone complete vagotomy. In the preoperative motility studies, gastric analyses after administration of insulin were carried out with

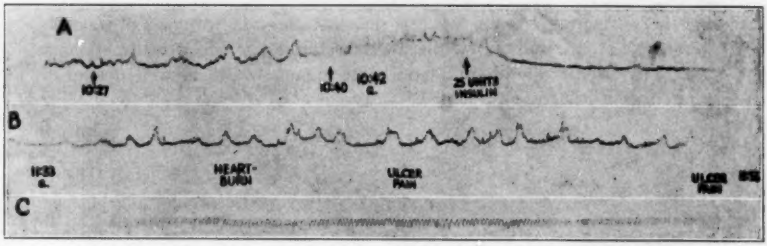

Fig. 4.—Record of gastric motility of patient S. V. *A*, preoperative record; 25 units of regular insulin was given intravenously as indicated on the graph. *B*, continuation of record *A* showing response of gastric motility to insulin hypoglycemia. *C*, postoperative record taken one week after subdiaphragmatic vagotomy.

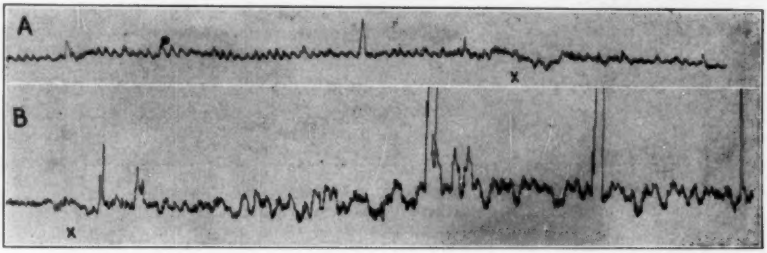

Fig. 5.—Gastric motility record of patient J. B. taken two weeks after subdiaphragmatic vagotomy. *A*, control record showing minimal gastric motor activity. The large excursion in the central portion of the record was produced by respiratory effort. Half a milligram of neostigmine bromide was given intramuscularly at *x*. *B*, marked increase in gastric contractions following subcutaneous injection of doryl® (0.25 mg.) at *x*.

simultaneous motility tracings in 2 patients, and the secretory response coincided with the motor response, as seen on the kymographic tracings.

CLINICAL DATA

From May 1946 to January 1949, 67 patients have been subjected to 69 vagotomies for peptic ulcer on the surgical service of the New York Hospital. These patients have been followed for one to twenty-eight

months in the outpatient department. Forty-nine patients have been followed for more than six months.

The general indications for operation have been (1) marginal ulcer with or without hemorrhage and (2) duodenal ulcer not responding to conservative management. In the consideration of vagotomy as an experimental procedure in the treatment of ulcer, the cases of duodenal ulcer were individually selected for a trial of this operation. In general the manifestations of hemorrhage and obstruction were deemed to contraindicate vagotomy. Gastric ulcer was felt not to be suitable for treatment by simple vagotomy.

Vagotomy was performed for duodenal ulcer in 44 patients, marginal ulcer in 23, gastric ulcer in 1 and esophageal ulcer in 1 (table 1). Recent significant hemorrhage from peptic ulceration had occurred in 14 of these patients, 8 of whom had marginal ulcers.

TABLE 1.—*Results of Section of Vagus Nerves*

	Location of Ulcer									
	Duodenal		Jejunal		Gastric		Esophageal		Totals	
Operation	No.	Failures	No.	Failures	No.	Failures	No.	Failures	No.	Failures
Transthoracic vagotomy	6	3	13	3	0	0	1	0	20	6
Subdiaphragmatic vagotomy only	22	3	8	3	0	0	0	0	30	6
Vagotomy and gastroenterostomy	12	0	0	0	0	0	0	0	12	0
Vagotomy and gastric resection	4	0	2	0	1	0	0	0	7	0
Total	44	6	23	6	1	0	1	0	69	12

The series consisted of 58 men and 9 women. Their ages ranged from 19 to 66 years, the average age being 43.5 years. A transthoracic approach was used in 20 cases, and subdiaphragmatic section was performed in the remaining 49. Two patients were operated on twice; in 1 case both operations were by transthoracic approach, and in the other the first was carried out subdiaphragmatically and the second through the chest. Other gastric operations were combined with vagus section in 19 patients. Gastroenterostomy was combined with vagotomy in 12 and gastric resection in 7.

Determinations of continuous overnight secretion were obtained in 45 patients, the volume ranging from 150 to 2,600 cc., with an average of 784 cc. preoperatively. In 44 patients determinations of night secretion were made after operation and the volumes varied from 50 to 1,000 cc., with an average of 397 cc. In general there was a decreased response to histamine in the immediate postoperative period, and in 7 patients achlorhydria was recorded. Failure of response to insulin was used as an indication of the complete division of the vagus. In 44 patients insulin gastric analyses after operation demonstrated complete vagotomy.

In 4 cases the tests were inconclusive in that the blood sugar level remained above 50 mg. or because of insufficient data or some other technical difficulty, and in 6 incomplete vagus section was demonstrated.

RESULTS

The results obtained by vagus section in this series are recorded in tables 1 and 2. Of those patients on whom transthoracic vagotomy was performed, 14 are considered to have satisfactory results by virtue of being free of ulcer pain. The operation in 6, or 30 per cent, is considered to have been a failure, and they have recurrent symptoms of ulcer. The latter group includes 1 patient in whom two unsuccessful attempts were made to perform complete vagus division. Forty-two patients obtained satisfactory results from transabdominal vagotomy, and in 24 of these the operations were confined to division of the vagus nerves without additional gastric procedures. The 6 patients in this

TABLE 2.—*Results of Vagus Section*

Operation	Number of Cases	Good Results	Failures	Percentage of Failures
Transthoracic vagotomy	20	14	6	30
Subdiaphragmatic vagotomy only	30	23	6	20
Vagotomy and gastroenterostomy	12	12	0	0
Vagotomy and gastric resection	7	7	0	0
Total	69	56	12	17.4

group in whom the operation failed also underwent vagotomy only. Thus there have been twelve failures in 69 vagus sections, or 17.4 per cent poor results (table 2).

In the 14 instances in which operation was performed on patients who had a recent episode of gastrointestinal bleeding hemorrhage has not recurred.

The patient with peptic ulceration of the esophagus has shown a progressive gain in weight since operation and is considered to have had a good result. This patient, a 23 year old man, had undergone two cardioplasties for cardiospasm, and then symptoms of peptic ulcer developed associated with moderately severe bleeding. Esophagoscopy showed ulceration of the lower part of the esophagus. Conservative therapy was unsuccessful, and there has been no return of symptoms ten months after vagotomy.

Secondary operation has been required in 6 patients. Gastroenterostomy was necessary twice because of continued gastric retention. In 1 of these patients vagus section was incomplete as demonstrated by a prompt and high secretory response to insulin hypoglycemia. One secondary operation was lysis of adhesions which caused intestina

obstruction in a patient three months after subdiaphragmatic vagotomy. Gastric resection has been performed for recurrent duodenal ulcer in 3 patients.

A 56 year old white man underwent transthoracic vagotomy on Dec. 16, 1946, for chronic duodenal ulcer. The preoperative night secretion was 650 cc. and gastric analysis after administration of insulin gave a maximum response of 38 units of free acid. After vagotomy the night secretion was 200 cc., and there was a maximum response of 15 units of free acid after administration of insulin. The patient was readmitted nine months later with intercostal neuralgia at the thoracotomy site and on Sept. 10, 1947, was subjected to section of the left seventh and eighth intercostal nerves, which gave relief. Studies of night secretion and gastric analysis with insulin at this time gave essentially the same results as immediately after operation. Fulness, occasional nausea and vomiting continued from the time of vagotomy until February 1948. Pain then slowly developed, and at operation on July 7, 1948, a large duodenal ulcer was found. The patient has remained asymptomatic since gastric resection.

A 42 year old man underwent transthoracic vagotomy on Jan. 29, 1947, for chronic duodenal ulcer. The preoperative night secretion was 900 cc., and gastric analysis after administration of insulin showed a maximum rise to 132 units of free acid. The postoperative night secretion was 1,000 cc., with no free acid after insulin was given. The patient obtained prompt relief of pain but had belching, fulness and diarrhea. The diarrhea lasted six months, and the fulness persisted until February 1948. He was asymptomatic until April 1948, when pain recurred. He was admitted to the hospital in August 1948 for gastric resection. The night secretion at this time was 1,300 cc., and gastric analysis after the use of insulin showed a response of 60 units of free acid. He has been asymptomatic since the performance of partial gastrectomy.

A 32 year old man underwent transthoracic vagotomy for chronic duodenal ulcer on Nov. 24, 1947. The preoperative night secretion was 800 cc. with 69 units of free acid, and gastric analysis after insulin was administered revealed a maximum rise to 99 units of free acid. The postoperative night secretion was 430 cc., with 68 units of free acid, and the postoperative insulin test showed falling values for acid, which were 68, 27, 10 and 10 units at fifteen minute intervals. The blood sugar content fell to 18 mg. per hundred cubic centimeters in forty-five minutes. The patient was asymptomatic until July 1948, when pain recurred. On his admission to the hospital in October 1948, the night secretion was 730 cc., and the insulin test showed a rise to 63 units of free acid. A large duodenal ulcer was found at the time of gastric resection, Sept. 16, 1948. He is now asymptomatic.

In all 3 of these patients repeated gastrointestinal roentgenograms showed no change in the deformed cap after vagus section.

Two deaths have occurred in the series. One patient died suddenly on the ninth day after operation from what seemed to be a massive pulmonary embolus; however, permission for autopsy was not obtained. According to the gastric analysis made after insulin was given, vagus section was complete. The second death occurred three months after the patient's discharge, and the report from the hospital in which he died stated that he had suffered from a cerebral vascular accident. This patient had required secondary gastroenterostomy for retention after incomplete vagotomy.

There were ten complications in the group in which a transabdominal approach was used and four complications in the patients operated on through a transthoracic approach (table 3). It was felt early in the investigation that the indwelling gastric tube which was used routinely for four or five days after vagotomy was contributing to the incidence of pulmonary complications, and, accordingly, the tube was later frequently withdrawn for intervals of two to four hours during the day. The complication of hiatus hernia has been reported elsewhere.[54] One patient had intercostal neuritis after transthoracic vagotomy and required section of the seventh and eighth dorsal nerves nine months later to obtain relief. One patient had symptoms and roentgenologic evidence of achalasia after subdiaphragmatic vagotomy, which was transient and disappeared spontaneously one month later. Esophagoscopy demonstrated spasm of the lower part of the esophagus

TABLE 3.—*Complications After Vagotomy*

Transabdominal		Transthoracic	
Pulmonary embolism	3	Pleural effusion	2
Pleural effusion	2	Intercostal neuritis	1
Bronchopneumonia	1	Hemothorax	1
Hiatus hernia	1		
Purulent bronchitis	1		
Atelectasis	1		
Achalasia	1		
Total	10		4

but did not benefit the patient. This case is being reported elsewhere by Wilcox.[55]

In 2 patients pulmonary tuberculosis has developed since their discharge from the hospital; both have complete relief from symptoms of ulcer.

Undesirable side effects have occurred in 33 patients, 48 per cent, frequently even when gastroenterostomy or gastric resection was combined with the division of nerves. Twenty-eight patients had signs and symptoms of gastric retention as evidenced by anorexia, fulness and belching of foul-smelling gas. These symptoms usually subsided gradually and were no longer troublesome after four to six months; however, in 1 case this syndrome persisted for thirteen months. A history of diarrhea was elicited in the interrogation of 17 patients. This was usually transient and disappeared after three to four months, but 1 patient was bothered by this symptom for ten months after operation.

54. Beal, J. M.: Diaphragmatic Hernia Following Subdiaphragmatic Vagotomy, Surgery **24**:625, 1948.

55. Wilcox, R. S.: To be published.

In an effort to alleviate these disturbances, doryl® has been administered to 6 patients and urecholine® to 2. These drugs were found to be effective in relieving symptoms due to disturbed gastric motility and those due to diarrhea. Clinically the drugs were equally effective and were used interchangeably without apparent variation in the results. Two milligrams of doryl® or 10 mg. of urecholine® was given by mouth one half hour before meals, either two or three times a day, without untoward effect. Doryl® was used in 2 cases as a gastric secretagogue after vagotomy, and, although the patients had no response to insulin, there was an immediate and marked secretion of free acid.

COMMENT

Division of the vagus nerves, when complete, has been demonstrated to result in elimination of the cephalic phase of gastric secretion whereby

TABLE 4.—*Results of Vagotomy in 8 Series of Cases*

Series	Number of Cases	Sastisfactory Results	Unsatisfactory Results	Deaths
Dragstedt, L. R.: Am. Surg. **126**: 687, 1947	212	194 (91.5%)	18 (8.5%)	1
Harkins, H. N., and Hooker, D. H.: Surgery **22**: 239, 1947	36	32 (89%)	4 (11%)	0
Johns and Grose [33]	43	34 (80%)	7 (17%)	1
Grimson [19]	57	48 (84%)	8 (17%)	1
Meyer, K. A.; Rosi, P. A., and Stein, I. F.: Surg., Gynec. & Obst. **86**: 524, 1948	35	30 (86%)	4 (14%)	1
Miller and Olwin [44]	92	76 (82%)	3 (4%)	0
Weinberg, J. A.; Campbell, G. W., and Voelker, R. B.: J. Thoracic Surg. **17**: 743, 1948	60	56 (90%)	3 (5%)	1
Present Series	69	56 (81%)	12 (17%)	1

the night secretion, excessive in volume and acidity in the patient with ulcer, is diminished. The response of the secretory mechanism of the stomach to psychic stimuli such as emotional difficulties and tension is abolished. The completeness of vagotomy may be determined by the response of gastric secretion to insulin hypoglycemia. When the severance of the vagal innervation of the stomach is complete, the patient with peptic ulcer experiences prompt relief of pain without disturbances of other gastric stimuli, such as heat, cold or hunger. The operation is associated with a low mortality rate, as is apparent in table 4, which records 6 deaths in 688 cases, a mortality of 0.9 per cent.

Alterations of motor physiology of the gastrointestinal tract frequently follow division of the vagi, resulting in gastric atony and delayed emptying of the stomach. Our experiments have indicated changes in the motor pattern of the small bowel as well. Clinically these changes result in nausea, fulness, belching and diarrhea.

In the evaluation of vagus section in the therapy of peptic ulcer, two important aspects remain to be elucidated. The etiology of ulcer is

a difficult and complex problem as yet unsolved. The question remains to be answered of whether or not abolishing one phase of gastric secretion is enough to result in permanent cure of peptic ulcer.

The possibility that the vagus nerve may regenerate is suggested by 3 cases presented. Dragstedt [55a] does not believe that such regeneration occurs, and in replying to a question relating to this possibility, he asks if anyone has seen a case of spontaneous regeneration of the recurrent laryngeal nerve following injury during operation. His stand in this matter seems untenable in two ways: First, the intrinsic musculature of the larynx, which is striated, receives somatic motor fibers from the recurrent laryngeal nerves which have their origin in the nucleus ambiguus of the eleventh cranial nerve.[56] The behavior of somatic motor fibers cannot be compared with the visceral motor elements concerned with gastric function. Second, the autonomic nervous system in other parts of the body is well known for its ability to regenerate.

Technically the surgical division of the vagus nerves is accomplished more easily than other operations performed in the treatment of peptic ulcer; however, the anatomic arrangement of the nerve fibers in the lower region of the esophagus presents a difficult problem. Well defined anterior and posterior trunks are encountered in most cases, but in some the numerous fibers render division of all uncertain. There appears to be a certain correlation between the clinical results in table 4 and the anatomic configuration of well defined nerve trunks discussed earlier in the paper. The surgeon thus must depend on laboratory tests in the postoperative period to determine whether or not division is complete.

Although the patient with ulcer may receive benefit from complete vagus section, the unpleasant side effects may detract from the desired result. Symptoms resulting from disturbed gastrointestinal physiology have been reported in as high as 67 per cent of cases, and gastric retention may require secondary operation.

The occurrence of diarrhea after vagotomy has not been adequately explained. Dragstedt's postulation that the diarrhea is of bacterial origin and due to loss of antiseptic action of free acid may be questioned, as the response of gastric mucosa to the second and third phases of gastric secretion is not abolished. Five patients in our series suffered from diarrhea after vagus section and at the same time were found to have 15 to 50 units of free acid after administration of histamine. That the changes in motility of the small intestine demonstrated in our experiments may have bearing on the occurrence of diarrhea seems likely. The pattern becomes irregular after vagus section, and the forward propulsion of the intestinal contents seems to be slowed. Peristalsis is not

55a. Dragstedt, L. R., in discussion on Dragstedt; Harper; Tovee and Woodward, Ann. Surg. **126**:708, 1947.

56. Mettler, F. A.: Neuroanatomy, St. Louis, C. V. Mosby Company, 1942.

entirely abolished, and it may be that the disturbance in motility results in an accumulation of intestinal contents until mechanical stimulation of the musculature of the small bowel produces a rather sudden ejection of the contents into the colon. Clinically it has been noted that the patients usually experience a feeling of "gas" or distention prior to the actual diarrhea. The favorable influence of doryl® and urecholine® on the diarrhea also supports the premise of this symptom being at least partly a response to alteration of the innervation in the small intestine.

In the evaluation of the results of vagotomy as a recent procedure in the surgical treatment of peptic ulcer, it must be judged by comparison with the standard procedures already in use. While it is fallacious to compare the results of an operation for ulcer based on follow-up studies of two years or less with results obtained from other procedures after a long term follow-up, some information may be gleaned from such comparison. In this clinic satisfactory results were obtained in about 98 per cent of patients with gastric ulcers treated by gastric resection and in about 90 per cent of patients with duodenal ulcers, these being based on studies of five and ten year periods following operation.[57] Cooper's recent paper [58] from this clinic showed an incidence of failures of 18.3 per cent from gastroenterostomy in the treatment of peptic ulcer, as compared with an incidence of 17.4 per cent immediately after vagotomy. Thus the immediate failures from vagotomy in our hands do not equal those after gastric resection and are more nearly similar to those after gastroenterostomy in a short term analysis. The results cited by others are in close agreement in general (table 4).

The place of vagotomy in the treatment of marginal ulcer appears somewhat more favorable. Six failures were encountered in twenty-three operations. Eight of the patients who had successful results had suffered recent significant hemorrhages from ulcer, and all these have remained asymptomatic without further bleeding since vagus section. Still another patient lends strong support to the efficacy of vagotomy in the treatment of marginal ulcer. He is a 54 year old man in whom marginal ulcer developed after gastroenterostomy in 1916. Between 1934 and 1942 he was subjected to four operations for recurring ulcer but without success. On Jan. 8, 1947, a transthoracic vagotomy was performed, and he has remained asymptomatic.

Simple vagotomy does not seem suitable for gastric ulcer because of the constant danger of malignancy. Allen and Welch [59] reported that of 23 patients with gastric ulcers treated by "conservative surgery" 4 died of cancer and that of 93 patients with a diagnosis of benign gastric ulcer

57. Cooper, W. A.: Personal communication to the authors.

58. Cooper, W. A.: End Results in the Treatment of Peptic Ulcer by Posterior Gastroenterostomy, Surgery **23**:425, 1948.

59. Allen, A. W., and Welch, C. E.: Gastric Ulcer: Significance of This Diagnosis and Its Relationship to Cancer, Ann. Surg. **114**:498, 1941.

treated by gastric resection 30 were proved to have cancer. Marshall and Welch,[60] in a series of 131 patients subjected to operation under the impression that they were suffering from benign gastric ulcer, found an error in diagnosis in 19.8 per cent. The first warning was by Latarjet [6b] in 1922, who performed vagotomy on 6 patients with gastric ulcers, 1 of whom died later of carcinoma. Unless the lesion is removed the danger of carcinoma exists.

Our case of esophageal ulcer that has so far responded favorably to vagus section suggests that the lesion may be amenable to this operation.

SUMMARY

The historical background of vagotomy has been briefly reviewed. The anatomy and physiology of the gastrointestinal tract as related to the treatment of peptic ulcer by division of the vagus nerves has been presented.

The results of experiments on dogs with particular reference to motility of the small intestine and the influence of vagus section have been discussed.

The results of vagotomy in the treatment of peptic ulcer in 67 patients have been reviewed, based on follow-up studies ranging from one to twenty-eight months. Satisfactory results in 81 per cent of the cases were reported. On the basis of our experience and the published results of others, the place of vagotomy in the treatment of peptic ulcer has been discussed.

CONCLUSIONS

When vagotomy is complete, the cephalic phase of gastric secretion is abolished and the excessive night secretion of high acid content is eliminated. In most cases the ulcer will heal and the patient is relieved of ulcer pain and associated symptoms.

Complete vagotomy may be anticipated in 80 to 90 per cent of cases according to clinical and anatomic studies. Objection to the operation is based on uncertainty of complete division of all fibers and on the undesirable side effects which accompany the procedure in a high percentage of cases. The permanency of benefits from vagus section is not yet established and must await the demonstration of the power of the vagus nerve to regenerate after division and of the ultimate place of the cephalic phase of gastric secretion in the pathogenesis of ulcer.

The results obtained with vagotomy in the treatment of duodenal ulcer are inferior to those from gastric resection. Simple vagotomy is contraindicated in cases of obstructing duodenal ulcer and of gastric ulcer. In the therapy of peptic ulcer, vagotomy seems best suited for marginal ulcer.

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60. Marshall, S. F., and Welch, M. L.: Results of Surgical Treatment for Gastric Ulcer, J. A. M. A. **136**:748 (March 13) 1948.

FAILURE OF VAGOTOMY TO PREVENT THE FORMATION OF MANN-WILLIAMSON ULCERS IN DOGS

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THE MANN-WILLIAMSON procedure of internal duodenal drainage is recognized as a convenient and consistent method of producing experimental peptic ulcers.[1] In from 90 to 100 per cent of dogs so prepared chronic progressive ulcers resembling the spontaneous ulcers of the stomach and duodenum in man develop. The availability of an experimental procedure which leads to the development of a specific disease in such a high percentage of cases obviously provides a most useful test object for the therapeutic effectiveness of various types of treatment. While this method was not employed by Dragstedt and his associates [2] when they introduced complete gastric vagotomy for the treatment of peptic ulcer in man, it has since been employed almost simultaneously in a number of different laboratories as a check on results coming from the clinic. During the progress of the present study, several workers have published results from similar experiments.

Harkins and Hooker [3] reported that the incidence of Mann-Williamson ulcers in dogs was markedly decreased by complete vagotomy. On the

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1. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409, 1923; Experimentally Produced Peptic Ulcer, S. Clin. North America **5**:753, 1925.

2. Dragstedt, L. R., and Owens, F. M., Jr.: Supra-Diaphragmatic Section of the Vagus Nerves in Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152, 1943.

3. Harkins, H. N., and Hooker, D. H.: Vagotomy for Peptic Ulcer: Experimental and Clinical Studies, Surgery **22**:244, 1947.

other hand, Saltzstein and his associates [4] noted little evidence of protection from this operation. In 6 of 8 dogs ulcers developed, as compared with a 100 per cent incidence in the control series. Oliver [5] observed no difference between the Mann-Williamson controls and the series in which additional vagotomy was carried out. It is interesting that in 1931 Beaver and Mann [6] performed the same experiment. The Mann-Williamson operation was performed on 9 dogs, 3 were kept as controls, the splanchnic nerves were sectioned in 3 and the vagi were divided in 3. Ulcers developed in all the animals except 1 in the group which had undergone vagotomy.

EXPERIMENTAL METHOD

The animals employed were pound dogs that were separately maintained for several days to a few weeks in order to improve nutritional status and to assure freedom from preexisting respiratory infections. These animals were then divided into two groups, i. e., experimental (A) and control (B). The dogs in group A were first subjected to a transthoracic vagotomy under intratracheal ether anesthesia, and about two or three weeks later a modified Mann-Williamson procedure was performed on the survivors. The original Mann-Williamson procedure was modified in that the pylorus and a small part of the antrum were either resected or excluded, a side to end gastrojejunostomy opening 3 or 4 cm. in length thus being permitted. This modification was designed to eliminate the nozzle-like action of the pylorus, which has been thought to play a part in the development and particularly in the location of Mann-Williamson ulcers on the jejunal mucosa. The Mann-Williamson operation without preceding vagotomy was performed in the control group (B). In the first 10 dogs of the vagotomized group and the first 9 of the control group, the stomach was transected about 2 cm. proximal to the pylorus and the distal portion infolded, the pylorus and a collar of antrum being left in continuity with the duodenum. The pylorus and about 2 cm. of antrum were resected in the remaining dogs of both groups and the duodenal end infolded. In either instance it was assumed that the small amount of antrum sacrificed would not appreciably affect results.[7]

The jejunum was transected at the first loop beyond the ligament of Treitz, and the distal loop was anastomosed with the stomach and the proximal loop with the ileum at an average distance of 25 to 35 cm. from the cecum. This procedure was altered slightly for dog no. 15 in group A, in which the vagotomy was done thirty-two days after the Mann-Williamson operation, and for dog no. 16 in group A, in which the two operations were performed simultaneously.

Postoperatively both vagotomized and control groups were given as nearly identical care as possible. Oral feedings were withheld and parenteral alimentation

4. Saltzstein, H. C.; Sandweiss, D. J.; Hammer, J. M.; Hill, E. J., and Vandenberg, H. J.: Effect of Vagotomy on Mann-Williamson Ulcers in Dogs, Arch. Surg. **55**:130 (Aug.) 1947.

5. Oliver, J. V.: Effect of Vagotomy on the Development of Mann-Williamson Ulcer in the Dog, Arch. Surg. **55**:180 (Aug.) 1947.

6. Beaver, M. G., and Mann, F. C.: Production of Peptic Ulcer after Section of Gastric Nerve, Ann. Surg. **94**:1116, 1931.

7. Lewis, E. B.: Acidity of the Gastric Contents after Excision of the Antral Mucosa, Surgery **4**:692, 1938.

employed for the first four postoperative days. The dogs were then placed on a normal dog diet, with ground beef or horse meat daily. Although it was intended to permit all dogs to live out their life spans, in three instances it was necessary to kill the animals because of severe inanition. The deaths of the animals of both groups that failed to survive the Mann-Williamson procedure by more than ten days were classed as postoperative deaths and therefore not reported in the series.

TABLE 1.—*Results of Vagotomy on Dogs with Mann-Williamson Ulcers*

Dog No.	Survival Time, Days	Weight Loss, Percentage	Number of Ulcers	Cause of Death
1	64	53	0	Malnutrition
2	24	18	1	Peritonitis (killed)
3	115	38	3	Peritonitis
4	106	32	2	Peritonitis
5	47	47	0	Malnutrition
6	59	19	5	Peritonitis
7	53	43	1	Peritonitis
8	87	48	0	Malnutrition
9	69	42	0	Pneumonia
10	144	26	0	Malnutrition
11	29	38	0	Malnutrition
12	74	47	1	Pulmonary edema
13	68	40	0	Pneumonia (killed)
14	49	38	0	Pneumonia (killed)
15*	59	56	0	Pneumonia
16†	25	28	0	Pneumonia
17	12	28	0	Unknown

* Vagotomy was performed thirty-two days after the Mann-Williamson operation.
† Vagotomy and the Mann-Williamson operation were performed simultaneously.

TABLE 2.—*Results in Dogs with Mann-Williamson Ulcers Used as Controls*

Dog No.	Survival Time, Days	Weight Loss, Percentage	Number of Ulcers	Cause of Death
1	11	31	0	Malnutrition
2	55	52	2	Peritonitis
3	38	9	2	Peritonitis
4	22	25	1	Peritonitis
5	67	56	3	Malnutrition
6	31	42	0	Malnutrition
7	64	38	1	Peritonitis
8	65	48	3	Peritonitis
9	35	35	1	Peritonitis
10	11	..	0	Pneumonia
11	18	..	0	Evisceration
12	46	..	1	Malnutrition
13	31	49	1	Malnutrition

RESULTS

Of the 17 dogs (table 1) that survived both the vagotomy and the Mann-Williamson procedure, chronic stoma ulcers developed in 6, or 35 per cent, and the average length of survival was sixty-four days. In contrast, in the control group of 13 dogs not subjected to vagotomy (table 2), ulcers developed in 9, or 69 per cent, with an

average period of survival of thirty-eight days. If one considers only those dogs surviving the Mann-Williamson procedure by more than three weeks, the earliest time of expected ulcer formation, ulcers developed in 90 per cent of the control dogs but in only 38 per cent of the vagotomized series.

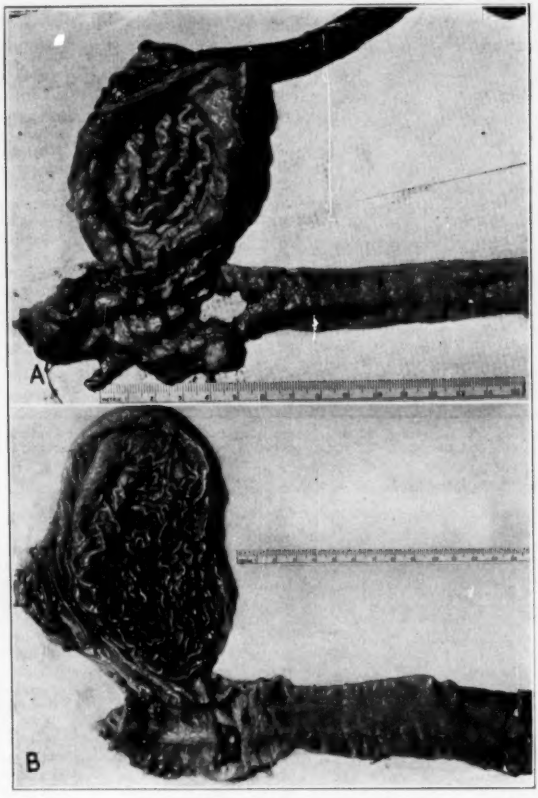

Fig. 1 (dog no. 2, group A).—*A*, this gross specimen of the stomach and jejunum contains a large perforating stomal ulcer which is typically located directly opposite the gastrojejunostomy opening. *B*, a gross specimen demonstrating another solitary stomal ulcer of typical location which contains two small perforations in its base.

At autopsy the stoma ulcers found were of the subacute type, with only moderate attempted repair, which often perforated and caused the death of the animal (figs. 1 to 5). The ulcers were nearly always

located on the posterior jejunal wall or near the junction at the greater curvature. In only 1 case did the ulceration extend into the suture line. Multiple ulcerations of the jejunum occurred nearly as commonly as the solitary lesions. Diffuse inflammatory changes in the upper jejunal mucosa were observed in over a third of the animals in the vagotomized group and in at least one instance in the control group. Distinct and, in a few instances, profound changes in the liver were noted in the dogs of both groups. Focal necrosis, atrophy and fatty degeneration were changes that seemed compatible with the extreme cachexia of the animals. Deposits of blood and bile pigments were also seen in the livers of both groups and as yet are unexplained changes. The com-

Fig. 2 (dog no. 2, group B).—Multiple jejunal ulcerations and perforations are visible in this specimen. This was the only instance in the entire series in which one of the ulcers involved the anastomotic suture line. The jejunal mucosa appeared grossly thickened and granular.

pletion of the vagotomy was confirmed at autopsy except in dog no. 12 of group A, in which about 50 per cent of the left vagus nerve had unintentionally been left intact.

COMMENT

It is apparent from these studies, as well as from those reported elsewhere, that gastric vagotomy does not protect animals appreciably from the formation of stoma ulcers after the Mann-Williamson procedure. The difference in survival time between group A and group B is not statistically significant. It is noteworthy, however, that the incidence of ulcer formation in those animals in group A in which the pylorus was excluded is four times greater than that in the remainder of the group, in which the pylorus was resected. This is of interest

in view of the similar high incidence of gastrojejunal ulcers in man following gastric resection with exclusion of the antrum, as in the method described by Finsterer and Devine.

At first glance, the failure to observe a protective effect of vagotomy on the Mann-Williamson ulcer in dogs appears contradictory to the fact now well established that similar vagotomy regularly causes gastrojejunal ulcers in man to heal and remain healed for long periods.[8] In the experience of one of us (L. R. D.) such ulcers have remained healed, and the period of observation has extended from two to five years. If, however, the factors that have been demonstrated to cause ulcers are kept clearly in mind, it is apparent that there is a crucial

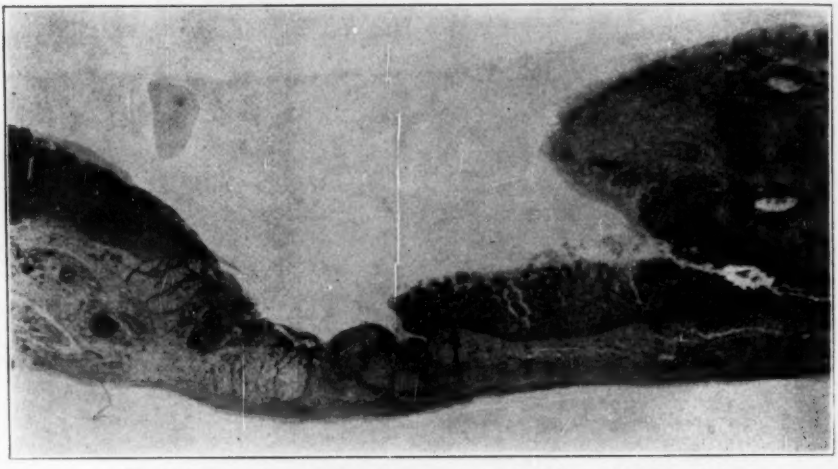

Fig. 3 (dog no. 9, group A).—Microscopic section of a typical jejunal ulcer demonstrating attempted healing with marked epithelization of the crater base. × 10.

difference between the Mann-Williamson ulcer as it is produced in dogs and the stoma ulcers which appear in man after gastroenterostomy or gastric resection. These operations are usually done for the treatment of duodenal ulcer, and it is now clear that the chief cause of such ulcers is excessive secretion of gastric juice in the interdigestive periods. Dragstedt, Palmer, Schafer and Hodges [9] have demonstrated that this

8. Dragstedt, L. R.; Clarke, J. S.; Harper, P. V., Jr.; Woodward, E. R., and Tovee, E. B.: Supra-Diaphragmatic Section of the Vagus Nerves to the Stomach in Gastro-Jejunal Ulcer, J. Thoracic Surg. **16**:226, 1947.

9. Dragstedt, L. R.; Palmer, W. L.; Schafer, P. W., and Hodges, P. C.: Supra-Diaphragmatic Section of the Vagus Nerves in the Treatment of Duodenal and Gastric Ulcers, Gastroenterology **3**:450, 1944.

hypersecretion is neurogenic in origin and is mediated by the gastric secretory fibers in the vagus nerves. Gastroenterostomy and gastric resection do not abolish this nervous hypersecretion, and the jejunal mucosa is thus exposed to its corrosive effect. Although the neutralizing duodenal secretions are present in the region of the anastomosis and exert an undeniable protective effect, this is not sufficient when

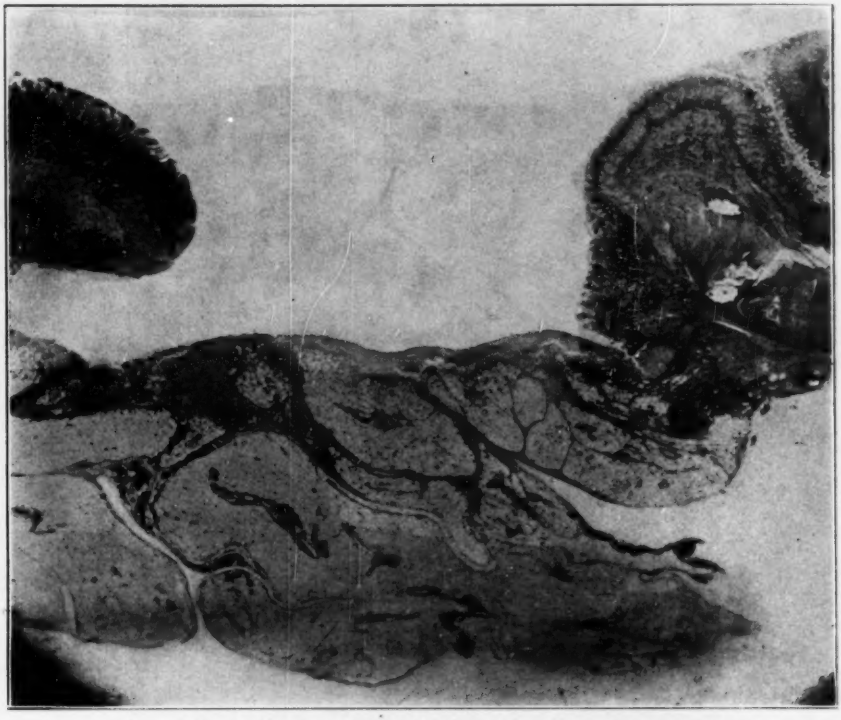

Fig. 4 (dog no. 12, group B).—In this jejunal ulcer from a Mann-Williamson control dog there is less evidence of healing than in the one in figure 4, and adherent omentum is seen on the serous surface adjacent to the deeply excavated cavity. × 10.

hypersecretion of gastric juice occurs although entirely adequate in the presence of a normal secretion. The failure of stoma ulcers to develop in normal dogs, or in man in the presence of gastric ulcer or carcinoma, after gastroenterostomy is evidence for the latter statement. Gastric vagotomy abolishes the nervous hypersecretion in patients with duo-

denal ulcers and reduces the secretion to normal or subnormal levels, and for this reason stoma ulcers do not develop when a gastroenterostomy is performed as an accompanying procedure. When a Mann-

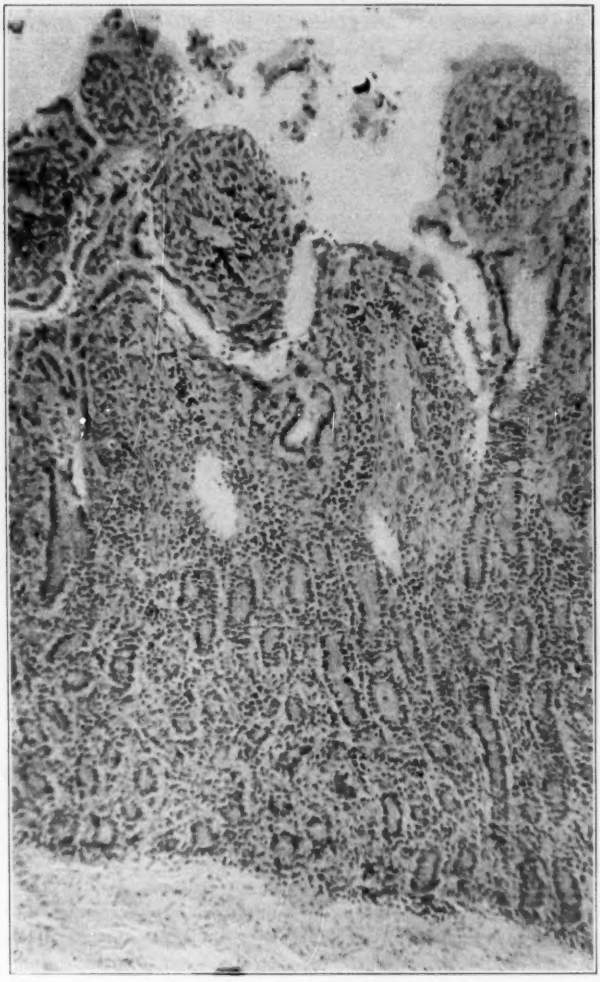

Fig. 5 (dog no. 1, group A).—A section of jejunum which appeared grossly granular and had thickened mucosa. The intestinal villi appear elongated, thickened and infiltrated with small round cells. There is a small amount of exudate on the mucosal surface × 128.

Williamson preparation is made, the situation produced is entirely different. The nervous phase of secretion is not exaggerated in the animals, and the ulcers produced result from the complete withdrawal of the alkalinizing duodenal secretions from the region of the anastomosis in the presence of a normal gastric secretion. Under these conditions, the removal of the nervous phase of secretion by vagotomy does not reduce the gastric secretion to the point where the jejunal mucosa can withstand its corrosive effect when entirely deprived of the duodenal secretions. Reflections such as these suggest that the Mann-Williamson experiment does not reproduce the disturbance in gastric physiology which is responsible for ulcers in man and accordingly is not an entirely adequate preparation for the assay of the value of antiulcer therapy.

Whereas duodenal and gastrojejunal ulcers in man are not strictly comparable to the Mann-Williamson ulcers in dogs in the sense that the duodenal secretions are completely diverted from the region of the anastomosis in the latter but not in the former, nevertheless there are certain instances in which ulcers of the Mann-Williamson type do occur in man. Owens [10] has recently described several cases in which these lesions developed after radical pancreatoduodenectomy. In these cases the pancreatic secretion was excluded by ligation of the ducts and the bile was diverted into the intestines at some distance below the gastroenterostomy stoma.

Many years ago Exalto [11] demonstrated that a gastroenterostomy of the Y or Roux type leads to the development of stoma ulcers in a high percentage of cases, both in man and in experimental animals. These are obviously similar in pathogenesis to the experimental ulcers of Mann and Williamson. The following recent experience illustrates the recurrence of a stoma ulcer following gastroenterostomy, in which the duodenal secretions were diverted from the region of the anastomosis, and the failure of complete gastric vagotomy to afford protection.

REPORT OF A CASE

The patient, A. V., was a 49 year old male chauffeur who was first seen in March 1947, when he complained of postprandial distress of the ulcer type for the previous twenty-one years. He was operated on in 1926, and a perforated duodenal ulcer was found and closed. A posterior gastroenterostomy was performed in 1928 and was followed by complete relief for two years. Since 1930 he has had almost constant distress with only partial relief from the intake of milk and alkalis. During the past year vomiting has become frequent and troublesome. Fluoroscopic examination revealed marked deformity of the duodenal bulb with obstruction. A stoma ulcer was not seen, but the proximal limb of the gastroenterostomy stoma

10. Owens, F. M., Jr.: Personal communication to the authors.

11. Exalto, J.: Ulcus jejuni nach Gastroenterostomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911.

was dilated and partially obstructed. A positive secretory response to insulin hypoglycemia was obtained, and the night secretion of gastric juice was 1910 cc. with a free acid value of 33 clinical units, 2,600 cc. with 8 units, 1,460 cc. with 21 units and 1,200 cc. with 30 units. On April 1, 1947, an exploratory laparotomy revealed scarring and deformity of the duodenum, a patent gastroenterostomy stoma with puckered scar in the jejunum near the anastomosis and obstruction to the proximal limb of jejunum in the region of the jejunal ulcer, with considerable dilatation and hypertrophy. To relieve this obstruction an enteroenteroanastomosis was made between the proximal and distal loops of jejunum, the mediastinum was opened and the vagus nerves divided about 3 cm. above the diaphragm. Convalescence was uneventful, and fluoroscopic examination in August 1947 failed to reveal an ulcer. He remained free from distress on an unrestricted diet until December 1947, when he was readmitted to the hospital because of profuse hemorrhage. This was controlled by medical management and blood transfusions. Fluoroscopic examination revealed an ulcer crater at the stoma. During the latter part of December three insulin tests were made, but in no case did free acid appear in the gastric contents. The night secretion was 490 and 580 cc. on two occasions, but with no free acid. Medical management was continued, and there has been no further bleeding to July 1948.

It is apparent that this patient had been subjected to a complete gastric vagotomy, as indicated by physiologic tests, but his jejunal ulcer failed to heal or promptly recurred after temporary healing. Previous experience,[8] which has revealed the effectiveness of complete vagotomy in causing stoma ulcers to heal, together with the experimental data in this study suggests that the recurrence in this case was due to the enteroenteroanastomosis, which diverted the duodenal secretions away from the gastrojejunal stoma.

SUMMARY AND CONCLUSIONS

Complete gastric vagotomy does not prevent the development of Mann-Williamson ulcers in dogs.

Complete gastric vagotomy does not protect against gastrojejunal ulcer in man when the duodenal secretions are diverted from the region of the stoma by an enteroenteroanastomosis between the proximal and distal limbs of the jejunum.

The inadequacy of the Mann-Williamson ulcer as a test object for the therapeutic effectiveness of antiulcer measures in man is discussed.

TREATMENT OF CHRONIC PANCREATITIS BY UNILATERAL SPLANCHNICECTOMY

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SINCE 1936 one of us has carried out several pancreatectomies on the left side with success in cases of limited pancreatitis involving the same side.[1] However, if the lesions are diffused throughout the pancreas, some other procedure has to be carried out. Total pancreatectomy, same side.[1] However, if the lesions are diffused throughout the pancreatitis with calcareous deposits but not in cases of chronic relapsing pancreatitis without stones in the duct of Wirsung. Frequent check of operations on the biliary tract in such cases induced one of us to perform unilateral splanchnicectomy in 1942.[3] From the first results, analyzed by Mallet-Guy and Vachon,[4] it was possible to see the importance of this method in the treatment of chronic pancreatitis.

In a recent paper, de Takats and Walter,[5] after having obtained excellent results in 2 cases, wondered whether the operation has not a direct effect on pancreatic lesions and whether it was possible to expect long-lasting results. We are now in a position to answer these two questions.

It is possible to report on 70 cases of splanchnicectomy for chronic relapsing pancreatitis (covering a period from March 20, 1942, to Sept. 14, 1948, taken from a list of 182 cases in which section was carried out for visceral disturbances.) The importance of this report lies in the results finally obtained by us in the study of the patients, several of them having been reexamined long after the performance of the operation.

From the Department of Surgery, University of Lyon.

1. Mallet-Guy, P.: Mém. Acad. de chir. **62**:559, 1936.

2. Whipple, A. O.: Ann. Surg. **124**:991, 1946.

3. Mallet-Guy, P.: Lyon chir. **38**:481, 1943.

4. Mallet-Guy, P., and Vachon, A.: Pancréatites chroniques gauches, Paris, Masson & Cie, 1943.

5. de Takats, G., and Walter, L. E.: Surg., Gynec. & Obst. **85**:742, 1947.

BASIS OF TREATMENT BY SPLANCHNICECTOMY

The use of this method is based on several arguments.

Physiologic Basis.—Vasomotoricity in the pancreas is controlled by splanchnic nerves, but the sensory supply of the pancreatic gland could not be ascertained in any way. It is possible to interpret the improvements clinically obtained as the effect of vasomotor changes resulting from the section of nerves. The experimental creation of acute pancreatitis through electric stimulation of the splanchnic nerve supports this,[6] and it is confirmed by the success obtained in the treatment of acute pancreatitis by splanchnic block.[7]

Thus far this action has not seemed to us to be specifically connected with one of the two splanchnic nerves, and our sections were carried out indifferently on the right or left nerve. Experiments on animals proved, however, that the right splanchnic nerve acts on the biliary ducts and the left splanchnic nerve on the pancreas. We therefore intend to verify later, by analyzing successes and principally failures, whether there exists any connection between the sectioned nerve and the result arrived at in man.

Physiopathologic Basis.—In many cases we had to admit, besides the obstructive or infectious biliary factor, the aseptic genesis of chronic pancreatitis because of the frequency and intensity of the nerve lesions in the presence of glandular sclerosis (as demonstrated by Martin, Mallet-Guy and Feroldi [8]) (fig. 1). Splanchnicectomy may be considered as effecting a vasomotor change which checks the development of inflammatory sclerosis or breaking the vicious reflex cycle responsible for acute or subacute recurrences.

Anatomic Basis.—The distribution of these lesions in the whole gland or in part of it, together with the incidence of related biliary lesions, constitutes another basis of the treatment.

The type of chronic pancreatitis which interests us here either involves the left side and is strictly limited to the body of the pancreas or is diffuse, with severe lesions on the left. In the first type, lesions of the biliary ducts, apart from functional disturbances, do not occur. In the second a certain response of the biliary flow may be added. In this category also falls chronic pancreatitis, affecting the left side, either an isolated lesion in the head or a diffuse process with lesions on the right side, without jaundice or stones in the common duct.

6. Mallet-Guy, P.; JeanJean, R., and Feroldi, J.: Lyon chir. **39**:437, 1944.
7. Marion, P.: Lyon chir. **40**:315, 1945.
8. Martin, J. F.; Mallet-Guy, P., and Feroldi, J.: Lyon chir. **38**:559, 1943.

In all cases the main part is played by the functional state of the biliary ducts, as the biliary effect of splanchnicectomy is proved beyond discussion both experimentally and clinically.[9] Lastly, the excellent results obtained in 72 cases of hypotonus of the gallbladder or the com-

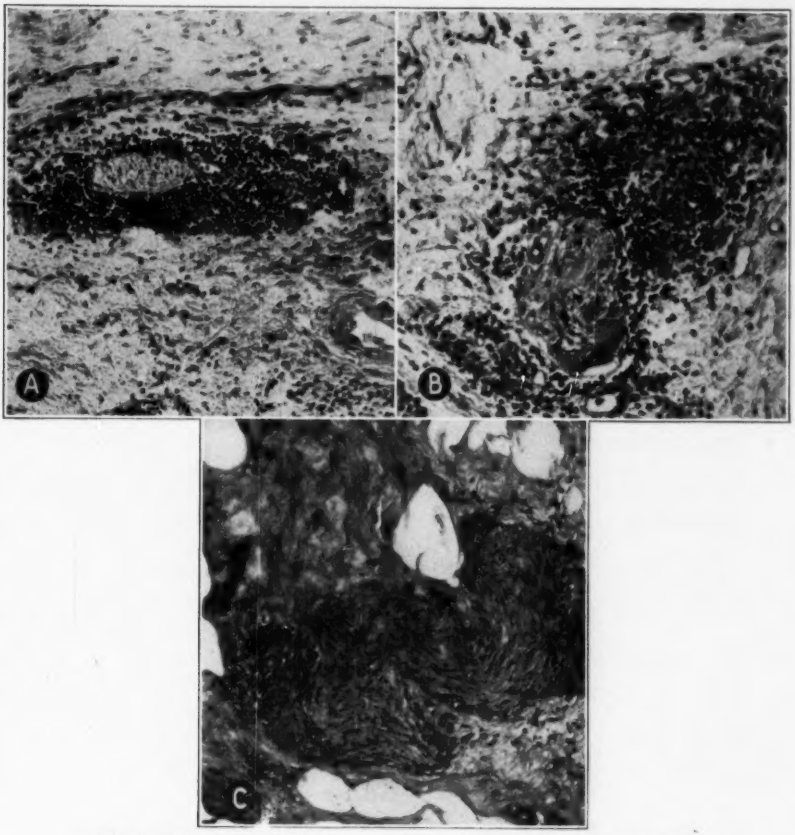

Fig. 1.—Chronic pancreatitis. *A*, perineural inflammation. *B*, perineural and endoneural inflammation and degeneration of some ganglion cells. *C*, enormous nerve; ganglion with cells very much distorted.

9. Mallet-Guy, P., and Guillet, R.: Lyon chir. **38**:436, 1943. Mallet-Guy, P., and Maillet, P.: Presse méd., 1941, p. 1385. Mallet-Guy, P., and Guillet, R.: Lyon chir. **38**:250, 1943.

mon bile duct [10] constitute a decisive clinical argument. At the same time they suggest vast possibilities in the treatment of the functional disorders of the biliary ducts, which were recorded in the referendum to the French Surgical Congress of 1947.[11]

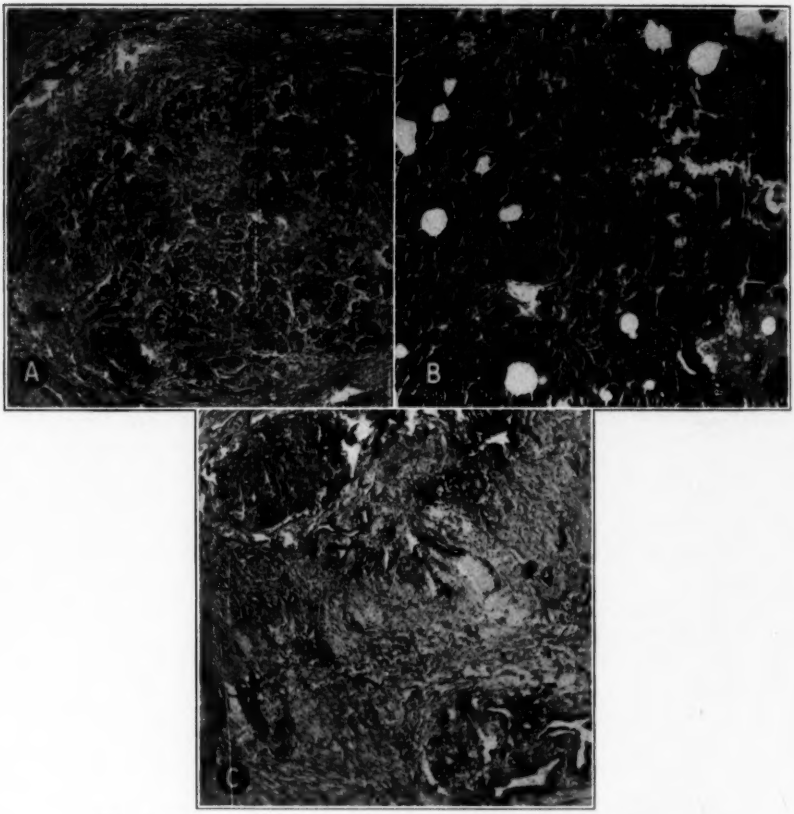

Fig. 2.—*A*, perilobular and intralobular sclerosis. *B*, microscopic appearance after recent hemorrhagic attack. *C*, dense, choking sclerosis.

This biliary effect can bring about failures whenever there exists a definitive degree of stenosis of the common duct or a hypertonic

10. Mallet-Guy, P., and Jaubert de Beaujeu, M.: Lyon chir. **43**:157, 1948.

11. Guillet, R.: Rapport au 50 ème Congrès de l'Ass. fr. Chir. 1947.

condition of the biliary ducts. Under these conditions, indications or contraindications to operation can be summarized as follows:

1. Hypertonus—splanchnicectomy contraindicated.

2. Compression—splanchnicectomy contraindicated in principle but may be performed after biliary anastomosis.

3. Normal biliary ducts—splanchnicectomy indicated.

4. Hypotonia—with frequent reflux in Wirsung's duct, splanchnicectomy indicated. Thus higher percentages of splanchnicectomies are performed for chronic pancreatitis involving the left side and the forms with hypotonus, with which the greater part of this report is concerned.

Clinical Basis.—In all cases it has been possible to define a clinical syndrome which appears most clearly in the cases in which the left side is involved and enables us to identify "left chronic pancreatitis." It consists of a group of painful and functional signs, the details of which are given in the chapter of results, since they form one of the basis for their evaluation. It also rests on a series of investigations verifying more or less authoritatively the clinical symptoms: (1) the detection of the painful left pancreatic spot, by the method described by one of us;[12] (2) laboratory tests evaluating the exocrin function of the pancreas, the results of which are not satisfactory, and (3) roentgenologic study, which may bring to light distortions of the duodenal curve, shows the enlargement of the duodenal loop with the softening of its angles, reveals the replacement or compression of the duodenal bulb and the antral area of the stomach and demonstrates the presence of pancreatic calcareous deposits.

To these typical signs of chronic pancreatitis are added the signs of biliary dysfunction, which may point, in the cases considered in this report, to disease of the gallbladder or the choledochus.

Provided with these data, which permitted us to diagnose with certainty the pancreatic lesion, we operated to investigate the exact place of the lesion and above all to examine the condition of the biliary ducts. This can be done only by manometric and roentgenologic control during operation, as we have systematically practiced it since 1942.[13]

OPERATIVE METHOD

Total thoracolumbar splanchnicectomy has not been performed because (1) actual results seemed satisfactory, (2) subdiaphragmatic splanchnicectomy is a simple operation, which can be carried out at

12. Mallet-Guy, P.: Presse méd., 1943, p. 170.

13. Mallet-Guy, P.; JeanJean, R., and Marion, P.: La chirurgie biliaire sous contrôle manométrique et radiologique per-opératoire, Paris, Masson & Cie, 1947.

the same time as laparotomy and (3) radical splanchnicectomy can always be performed if any indication is found, but bilateral splanchnicectomy comes first.

Splanchnicectomy is carried out in the subperitoneal lumbar region, after muscular dissection or resection of the twelfth rib, if this is long. The operation consists of excising the great splanchnic nerve for a length of 3 cm. at least and possibly dissecting some minor fibers under the light of an electric retractor as they pass through the diaphragm and sectioning them at the horn of the semilunar ganglion. The horn itself is not resected because it is useless and in some cases injurious and may cause trouble with intestinal peristalsis. We have never thought it necessary to resect the sympathetic trunks from which the splanchnic nerve originates.

ANALYSIS OF RESULTS

Analysis of the 70 cases shows the following results: There was 1 postoperative death. Observation was limited to less than one year in

TABLE 1.—*Data on 37 Cases in Which Observation Was Extended to More than One Year*

Results	> 1 Year	> 2 Years	> 3 Years	> 4 Years	> 5 Years	> 6 Years
Perfect	9	3	4	3	1	1
Very good	5	..	1	1	..	..
Good	1	..	1	1	..	..
Indifferent	..	..	..	..	1	..
Failure	5 cases	..	..	..	..	..

32 cases either because of loss of contact with the patient or because the operations were as yet too recently performed. Most of these recent operations were outright successes. Observation was extended to more than one year in 37 cases which were of interest to us, as table 1 shows. The functional results in these 37 cases were as follows: There were 5 failures, an incidence of 13.5 per cent; 1 indifferent result, 2.7 per cent, and 31 favorable results, 83.8 per cent. The lesions, surgically exposed, were often confirmed by pancreatic biopsy in the 31 cases. The favorable results were graded excellent in 21 cases (56.8 per cent), very good in 7 (19 per cent) and good in 3 (8 per cent).

Criteria of Improvement.—The healing process is characterized by an increase of weight, often important. This increase, pointed out by de Takats [5] (his patient had gained 29 pounds [13.2 Kg.] in two and a half months), is remarkable in respect to its degree and its rapidity, as may be seen in the early results since patients operated on two and three months previously showed increases in weight of from 4 to 10 Kg. Generally running parallel with the degree of improvement and

its persistence, the gain in weight often begins before the disappearance of functional difficulties.

Functional Disturbances: Diarrhea disappeared, which in several cases was the dominant symptom. There was disappearance of digestive troubles, such as difficulty in digesting certain kinds of food, heaviness in the epigastrium and the left hypochondriac region, and, in fact, all the chronic pain in the left and dorsolumbar areas, to which are added the acute paroxysmal attacks of pain.

We lay stress on these signs because the patients who came to operation had been suffering for several years and showed considerable emaciation; their attacks had increased in number and acuity, and some of them had experienced one or several attacks of acute pancreatitis which required a previous operation. These results are accompanied with a physical and moral transformation. All patients, even those whose recovery was not complete, agreed in saying that the intervention transformed their lives. They have started regular, sometimes even hard, work. The fact that some of them had already undergone one or even two operations for pancreatitis and that the lesions then found had not healed or even had progressed fully demonstrated the action of neurotomy on the evolution of anatomic lesions of pancreatitis.

The good results were not always obtained at once. In 15 of the 31 cases in which favorable results occurred, that is, in 48.3 per cent, all complaints disappeared at once; they never recurred up to the time of the last reexamination.

In the entire group the common duct was normal or, more often, widely open. This shows the importance of the condition of the biliary ducts when splanchnicectomy is being performed. Aware of this fact, in spite of an extremely good result, we performed cholecystogastrostomy soon after splanchnicectomy on a patient who showed a certain degree of compression of the lower end of the common duct. The result now is excellent, though the anastomosis is no longer patent.

In addition, it is remarkable to note that in two thirds of the cases of chronic pancreatitis, with hypotonic common bile duct, excellent results were at once obtained and that they are almost the only ones in which the results remained perfectly satisfactory.

The second group of cases in which there were good results (16, or 51.6 per cent) covers those in which temporary difficulties were at first present. In some attenuated signs of pancreatitis, i. e., slight pain on the left on palpation or, later, one or two slight attacks, generally due to excesses in diet, continued and then everything disappeared definitely. These attacks were never as long or as acute as those which occurred before surgical intervention.

The persistence of attenuated painful phenomena, often clinically demonstrated by the painful subcostal spot on the left, may be ascribed to pancreatic lesions. As these have developed over a period of years, creating irreversible histologic lesions (as shown by the biopsies performed), it is logical to think that they still appear after splanchnicectomy, especially if excesses in diet have required intense functional strain of the gland. The temporary persistence of painful postoperative phenomena is one of the proofs that this operation is not a symptomatic operation intended to relieve pain.

In other cases new symptoms occurred, centering in the biliary tract. Some were of an infectious origin, others were transitory and appeared as slight pains located in the right side of the hypochondrium, with headaches. We were clearly dealing with hypertonic biliary phenomena, since most of the symptoms occurred in patients showing disturbances of the common duct or, especially, in those whose biliary duct had not been investigated during operation. We are led to believe that they showed anatomic or functional disturbances, increased by splanchnic neurotomy. Often the phenomena disappeared under the effect of amyl nitrite or atropine or of duodenal aspiration. In other, fortunately rare, cases their intensity or recurrence required surgical intervention; in 1 case cholecystogastrostomy was carried out, with an excellent result.

CONCLUSIONS

In 83.77 per cent of cases observed by us splanchnicectomy resulted in remarkable improvements. This is the more striking since a certain number of patients had lesions which contraindicated all other methods of therapy or even had uselessly undergone a whole series of operations, usually performed for pancreatitis. Besides, there often existed (table 2) lesions of the gallbladder requiring at the same time definite cholecystectomy or temporary cholecystostomy. These we were able to perform at once, aware of the condition of the biliary tract.

Most of the satisfactory results were obtained in cases of chronic pancreatitis combined with hypotonic biliary ducts, which constitutes the best indication for splanchnicectomy.

The excellency of both immediate and late results contrasts splanchnicectomy with biliary operations in which results are often poor or transitory. Its mild character and simplicity often make it replace pancreatectomy on the left side, considered as a resection of lesions generating reflexes. Most important of all, splanchnicectomy affords possibilities of various kinds:

1. It is bilateral in character. During the postoperative period, or later, improvement in some patients was aided by block of the other

splanchnic nerve; 1 of our latest patients, who continued to show definite pancreatic disturbance, subsequently underwent resection of the remaining nerve and at once showed real improvement.

2. It leaves room for a limited resection (pancreatectomy on the left side), which is indicated on the failure of neurotomy or as a complement of it.

3. After an improvement in the condition of the biliary flow, obtained through drainage or anastomosis, in a case of infection or partial com-

TABLE 2.—*Data on 31 Favorable Results with Reference to Condition of Biliary Tract and Simultaneous or Subsequent Operation*

Condition of Biliary Tract	Type of Operation
Unexplored	7 splanchnicectomy only 1 splanchnicectomy and cholecystogastrostomy *
Normal	2 splanchnicectomy only
Normal common duct and cholelithiasis	2 cholecystectomy and splanchnicectomy
Hypotonia of gallbladder	2 splanchnicectomy only
Hypotonic common duct and cholelithiasis or cystic duct disease	1 cholecystostomy and splanchnicectomy 3 cholecystectomy and splanchnicectomy
Normal gallbladder	1 splanchnicectomy only
Hypotonia of gallbladder	9 splanchnicectomy only
Abnormal common duct with compression	1 splanchnicectomy only 1 cholecystostomy and splanchnicectomy * 1 cholecystostomy and splanchnicectomy plus cholecystogastrostomy

* Subsequent operation.

pression of the common duct or of slight hypertonia, it can be justified as a second stage in the treatment of a persisting pancreatic lesion.

Biliary anastomosis, justified when there is compression or an abnormal appearance of the choledochus, may assume a new importance as the first stage in treatment. But the limits of its application can be set only by means of an operative exploration of the pancreas and biliary ducts, which makes it possible to determine the nature of the lesions, test the biliary ducts, treat a combined biliary lesion and decide whether splanchnicectomy is indicated.

RETROGRADE JEJUNOGASTRIC INTUSSUSCEPTION

Report of a Case

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DESPITE its apparent infrequency, acute retrograde jejunogastric intussusception is a serious complication of gastroenterostomy unless recognized promptly and treated surgically. The first gastroenterostomy was performed in 1881, but it was not until 1917 that the first complication of this type was recorded by Steber.[1] Bettman and Baldwin [2] collected 33 cases in their comprehensive review of the subject in 1933, and since that time 17 additional cases have been reported. The following report of a typical case illustrates the necessity of early recognition of this condition.

REPORT OF A CASE

Z. P., a 55 year old white man, was admitted to the hospital on Sept. 26, 1947, with the chief complaint of severe pain in the upper abdominal region and vomiting. His first admission was in 1936, when a diagnosis of duodenal ulcer was made. Subsequently, his symptoms of gnawing epigastric pain, relieved by food, became progressively worse until April 1942, when a posterior gastroenterostomy was performed. After recovery from this operation, the patient had no gastrointestinal symptoms until the time of the present admission; he had, however, entered the hospital again in December 1943 with the complaint of headaches.

The present illness began on the day before admission, when the patient suddenly began having severe epigastric pain, intermittent in character and followed shortly by vomiting. At first the vomitus did not contain blood, but later it became dark red. Pains persisted, with vomiting recurring every two hours until his admission to the hospital.

On examination in the hospital the patient was seen to be an undernourished elderly man who presented signs of dehydration, abdominal distress and mild shock. The blood pressure was 90 systolic and 60 diastolic, the pulse rate was 95 and the temperature was 98.8 F. Abdominal examination revealed no masses, but there was increased resistance in the epigastrium. Laboratory examination

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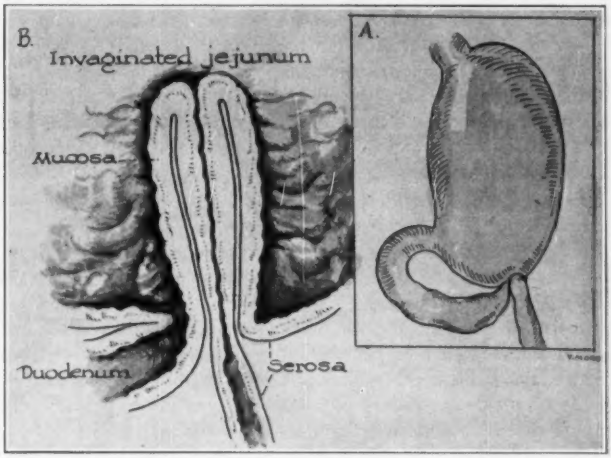
1. Steber: München. med. Wchnschr. **64**:648-649, 1917.

2. Bettman, R. B., and Baldwin, R. S.: Retrograde Intussusception of Jejunum: Complication of Gastro-Enterostomy, J. A. M. A. **100**:1228-1229 (April 22) 1933.

on admission revealed a red blood cell count of 4,910,000 cells per cubic millimeter, a hemoglobin content of 12.9 Gm. and a white blood cell count of 22,000, with 82 per cent polymorphonuclear leukocytes.

On the evening of admission the patient continued to vomit from 400 to 800 cc. at a time. Some of the vomitus contained blood clots, and the remainder was dark reddish brown. Transfusions of whole blood were given liberally to maintain circulation. On the second day in the hospital the abdomen was tender and boardlike in rigidity. The clinical diagnosis at this time was perforated peptic ulcer with peritonitis. Despite numerous transfusions and infusions and large doses of penicillin, the patient gradually became irrational and died on the fifth day.

Postmortem examination, performed two hours after death, revealed the abdomen to be flat but rigid; no masses were palpable. When the peritoneal cavity was opened, the stomach appeared extremely dilated, extending downward to



Tumor arising out of the opening of a gastrojejunostomy

the crest of the ileum and displacing the small intestine into the pelvis. No free fluid or signs of peritonitis were found in the peritoneal cavity. At the site of an old posterior gastrojejunostomy both loops of jejunum were dilated and disappeared into the stomach. The stomach contained approximately 3,300 cc. of thin brownish fluid and a sausage-shaped tumor arising out of the stoma of the gastrojejunostomy (figure). This mass proved to be the efferent loop of the jejunum, which had become invaginated in a retrograde manner through the stoma of the gastrojejunostomy. The base of the intussusception was 10 cm. below the stoma, and the stomach contained over 20 cm. of gangrenous doubled jejunum. The duodenum was dilated, and areas of acute inflammation were seen in the gastric mucosa, but no tumor or ulceration was detected in the duodenum or at the stoma. There was complete obstruction of the gastrointestinal tract at the point of intussusception, but the remainder of the small and large intestine was collapsed.

COMMENT

The etiology of retrograde jejunogastric intussusception is unknown. Inasmuch as no tumor or ulceration of either stomach or jejunum has been found in the majority of cases (in contradistinction to intussusception and retrograde intussusception elsewhere in the gastrointestinal tract), the mechanical explanation of retrograde jejunogastric intussusception is not as reasonable as a dynamic concept. Drummond [3] has suggested a mechanism of powerful antiperistaltic activity of the jejunum irritated by the presence of acid gastric contents. Certainly, important factors in the production of this condition are relaxation of the gastric wall and violent jejunal antiperistalsis; predisposing factors include unusually large stoma, proximity of the afferent and efferent loops and sudden increase of intra-abdominal pressure, which forces the jejunum upward. According to Oselladore,[4] who reproduced in dogs retrograde gastrogastric invagination by injection of weak isotonic silver nitrate solution into the wall of the stomach, the edema of the anastomosis "may cause active gastric peristalsis directed toward emptying itself more rapidly and this peristalsis may throw the gastric mucosa on the anastomosis initiating the invagination."

In Bettman and Baldwin's [2] 33 cases and in 13 additional cases [5] reported since 1933 the symptoms of the acute type of retrograde jejunogastric intussusception have been the sudden onset of severe, colicky, epigastric pain followed by persistent vomiting, at first clear but later frequently becoming blood tinged. The patient may be in moderate to severe shock, with signs of dehydration. In 17 of the 46 patients a mass could be palpated in the epigastrium, but tenderness and rigidity of the upper region of the abdomen were the only signs in 11. In 8 patients fulness and tenderness in the epigastrium were the only pertinent abdominal symptoms, and in 10 patients neither a mass nor rigidity was noted.

Laparotomy was performed on 32 patients for whom the result and the time of operation with reference to the onset of symptoms were known. Of the 19 operated on within forty-eight hours of the

3. Drummond, H.: Brit. J. Surg. **11**:79-88, 1923.

4. Oselladore, G.: Arch. ital. di chir. **53**:357-363, 1938.

5. (*a*) Adams, A. W.: Brit. M. J. **1**:248-250, 1935. (*b*) Chesterman, J. T.: Brit. J. Surg., **21**:541, 1934. (*c*) Debenham, R. K.: Brit. M. J. **1**:250, 1935. (*d*) Ducey, E. F., and McNamara, W. L.: Ann. Surg. **105**:461-463, 1937. (*e*) Gardaz, E.: Schweiz. med. Wchnschr. **66**:251-252, 1936. (*f*) Gottesman, J.: Intussusception of Jejunum Following Gastro-Enterostomy, J. A. M. A. **106**:1895 (May 30) 1936. (*g*) Greenwood, J. M.: Lancet **1**:266, 1937. (*h*) Pennefather, A. L.: J. Roy. Army M. Corps. **66**:193, 1936. (*i*) Poliquin, P. A.: Union méd. du Canada **73**:18-30, 1944. (*j*) Shackman, R.: Brit. J. Surg. **27**:475-480, 1940. (*k*) Weston, W. H.: Proc. Roy. Soc. Med. **39**:709, 1946.

onset of symptoms, 17 recovered, but of 13 operated on after forty-eight hours, only 7 recovered. The gross surgical mortality, therefore, was 25 per cent, whereas among those operated on within forty-eight hours the mortality was 10.5 per cent. All the patients who were not operated on died. In most cases the intussusception was readily reducible, but in 1 patient the invaginated portion of the jejunum was considered nonviable, and resection of the loop and a portion of the stomach was required.

In addition to acute retrograde jejunogastric intussusception, there have been reports of cases indicating a recurrent or chronic type of intussusception. Anatomically, there are three kinds of intussusception through the stoma of a gastroenterostomy. In the first type the afferent loop alone may enter the stomach; signs and symptoms may suggest subacute intestinal obstruction. In the second type the reverse intussusception begins in the efferent loop and enters the stomach, and obstruction is complete. In the third type both afferent and efferent loops become invaginated through the stoma. This may represent the end result of either of the first two, but symptoms and signs should be suggestive of acute high intestinal obstruction.

Clinical evidence of chronic intermittent intussusception has been presented by Sibley,[6] Adams,[5a] Gutmann,[7] Chamberlin[8] and Butler and his associates.[9] In each instance symptoms consisted of intermittent episodes of epigastric pain, nausea and vomiting, which subsided spontaneously. Diagnosis was made by fluoroscopic and roentgenographic demonstration of a filling defect in the stomach, which was movable on palpation, with a uniform pattern of parallel curved lines suggestive of jejunal mucosa. In Sibley's and Chamberlin's series no intussusception was encountered at operation, but in the case reported by Butler and his co-workers invagination of the jejunum was present.

The differential diagnosis of both acute and chronic retrograde jejunogastric intussusception must include peptic ulcer with hemorrhage or peritonitis, high intestinal obstruction due to adhesions or tumor, disease of the biliary tract and acute pancreatitis. The diagnosis should always be considered for a patient who has undergone previous gastrojejunostomy and subtotal gastrectomy and who has symptoms of sudden severe epigastric pain, repeated bloody vomitus and a palpable epigastric mass or tenderness over the epigastrium. That a similar complication may follow subtotal gastric resection, as reported by McNamara[10]

6. Sibley, W. L.: Proc. Staff Meet., Mayo Clin. **9**:364-365, 1934.
7. Gutmann, R. A., and Jobin, R.: Presse méd. **45**:923-925, 1937.
8. Chamberlin, G. W.: Am. J. Surg. **49**:510-512, 1940.
9. Butler, F. E.; Woolley, I. M., and Burton, W. Y.: Radiology **44**:498, 1945.
10. McNamara, W. L.: Ann. Surg. **120**:207-210, 1944.

leads one to expect no decline in the frequency of this complication, since this procedure has become increasingly popular in the treatment of gastric and duodenal ulcers.

SUMMARY

A case of retrograde jejunogastric intussusception following posterior gastroenterostomy performed five years previously for duodenal ulcer is reported. Review of the literature revealed 46 cases of acute and 5 cases of subacute or chronic retrograde invagination. The possibility of the latter complication must therefore be considered in the differential diagnosis of even the milder gastrointestinal complaints following gastric operation. Although there has been a 100 per cent mortality for the acute condition when surgical exploration was not attempted, early operation has proved life saving in 90 per cent of cases so far reported.

MALIGNANT TUMORS OF THE PARATHYROID GLANDS

A Review of the Literature with Report of a Case

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A MALIGNANT tumor arising in the parathyroid glands presents an appropriate topic for discussion because there has not yet been a common understanding among writers of what constitutes carcinoma of these glands. Usage in many instances of the piquing term malignant adenoma attests to this fact.

From the data given in many reports of cases in the literature, it is evident that the diagnoses were in error. The early reports of carcinoma showing no evidence of hyperparathyroidism are especially inconclusive. Carcinoma of the thyroid gland has been mistaken most often for a malignant tumor of the parathyroid glands. In more recent years, since there has been some understanding of the physiology and a better knowledge of the anatomic variations and cytology of these glands, it has been possible to come to a more definite opinion of the nature of the tumor. Analysis of the reports since 1902 of parathyroid tumors which functioned has been made possible because of the finding of a tumor in the neck or mediastinum which was associated with signs and symptoms of a disease compatible with hyperparathyroidism.

A small percentage of parathyroid tumors have been classified as malignant solely on the basis of changes in the appearance of the cells and their nuclei and in the arrangement of these cells within the tumor mass. This is particularly true in the review of a series of 14 cases of hyperparathyroidism presented by Alexander and others (1944), in which 13 (92.8 per cent) showed cytologic evidence of malignancy when Broders' standards were used. In at least 3 cases the tumor was reported to show adenocarcinoma of grade 2 malignancy. In 4 cases there was evidence of invasion of the capsule by neoplastic cells. In none of the descriptions of the microscopic examination of the tumor was invasion of the lymph or blood channnels mentioned. None showed metastasis or local recurrence. The authors expressed the opinion that such further

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evidence of the malignant nature of these cytologically malignant tumors might not have occurred because the duration of the disease to the time of extirpation of the tumor was relatively short, averaging 3.9 years. This was not considered a long period in the history of some low grade malignant tumors.

In striking contrast is the earlier (1941) report of Cope. He stated that in none of the 58 hyperfunctioning adenomas seen at the Massachusetts General Hospital was there evidence of malignant degeneration. He considered adenocarcinoma of the parathyroid glands a rare disease and stated that in no reported case had hyperfunction been proved. Partly on this premise he felt that subtotal resection rather than complete removal of the hyperfunctioning tumor was sometimes indicated in order to avoid life-endangering tetany. In only 1 of the 9 cases in which a subtotal resection of an adenoma was done had it been necessary to remove the remnant for residual hyperparathyroidism.

One of the cases in the series of Alexander and others had been reported previously (1936) by Snell. The tumor was considered cytologically to be a grade 1 adenocarcinoma. At some points there was apparent capsular invasion. In reference to the original account of this case, Cope stated that the report of carcinoma in a gland giving rise to hyperfunction was not beyond question but made no further comment. No account of the patient was given beyond seven months after the removal of the tumor, at which time he was in apparent good health. The serum calcium content was normal, and roentgenograms showed diminution of the degree of osteoporosis.

Another of the cases in the series had been reported separately by Wilder and Wellbrock in 1929. The tumor was removed in 1928. It was considered, also from the cytologic evidence, to be a parathyroid adenocarcinoma, grade 1. In several regions the neoplastic cells appeared to have invaded the capsule. The patient died in 1940 of carcinoma of the esophagus. Postmortem examination disclosed no evidence of recurrence or metastasis. The case was reviewed by Castleman and Mallory, who regarded the parathyroid tumor as an adenoma of the glandular and cystic type.

Concerning the 3 cases in their series which were classified as cases of adenocarcinomas of grade 2 malignancy, the cell changes were more marked and tumor giant cells were notably present. Observation postoperatively suggested correction of the hyperparathyroid state. The patients were dismissed feeling well in from three to six weeks. There was no record of further follow-up.

The authors stated that cytologic evidence of malignancy was seen in chief cells, oxyphil cells and wasserhelle cells. It included "irregularity of size and staining power of nuclei, a densely staining chromatin

network, giant nuclei, mitotic figures, pathologic mitoses, prominent nucleoli, irregular cellular arrangement, and invasion of the capsule and blood vessels by tumor cells" (Alexander and others).

In discussing their report, Mandl stated that their classification of malignant parathyroid tumors was purely a microscopic one since clinically there were no indications of malignancy. It seemed worth while to him to subject the clinical picture as well as the microscopic findings to closer analysis.

Reports of cases of parathyroid tumors, functioning and nonfunctioning, which present convincing evidence of their inherently malignant nature are indeed few. In these cases there has been invasion of the capsule and contiguous structures, including the blood and lymph channels, usually with postoperative recurrence. Distant metastasis has been rare (Hall and Chaffin; Meyer and Ragins).

NONFUNCTIONING MALIGNANT PARATHYROID TUMORS

Guy in 1929 reported the excision of a fairly well demarcated parathyroid tumor which grossly and microscopically appeared benign. A few nests of epithelial cells were contained in the capsule. The patient noticed another mass growing in the neck one week after discharge from the hospital. Within the year several separate cervical tumors had appeared. These were excised and were found to be of parathyroid origin. The cells had acquired malignant characteristics and had invaded the capsule and the lymphatic channels. About two and one-third years from the initial operation there was evidence of pulmonary metastasis. The patient left the city, and the further course could not be followed.

In 1932 Price and Mowatt reported the partial excision of a malignant tumor of the neck which they believed had arisen from a parathyroid rest. The patient had noticed a small lump, which after eight years began to grow rapidly. Grossly the tumor showed infiltrative characteristics, and histologically the cells resembled malignant parathyroid more nearly than any other malignant tissue likely to arise in this region. The patient died about nine months postoperatively from the spreading tumor and metastatic growths. A postmortem examination was not performed.

In 1938 McQuillan reported the removal of a parathyroid tumor which was firmly adherent to the trachea. Two years later a recurrent nodule attached to the external jugular vein was excised. The patient received roentgen therapy. There was further recurrence at the site of excision, and, somewhat removed, another more superficial nodule appeared. The author stated that the diagnosis of a malignant growth had been based on metastasis rather than on the characteristics of

individual cells. The microsection had disclosed capsular invasion. The pathologic diagnosis was adenoma of the parathyroid glands. The subsequent course of the patient was not recorded.

In 1934 Hall and Chaffin reported the removal of a parathyroid tumor along with a cystic tumor of the thyroid. Histologically the new growth appeared benign. Sixteen months postoperatively three nodules were evident in the neck and were excised. They were of parathyroid origin and showed gross and microscopic evidence of invasion of the muscle. There was also tumor cell invasion of the blood vessels. The patient died seven years after the first operation, and necropsy disclosed metatasis to the lungs and tracheobronchial lymph nodes.

The report of Toland in 1931 of a case of adenocarcinoma of the parathyroid glands and death four months postoperatively after pulmonary metastasis is not entirely convincing from a study of the data given. Hall, who examined the microsections, believed that the tumor was of parathyroid origin and that malignancy was established on the basis of the rapidly fatal course. There was no record of a postmortem examination.

The case reported in 1927 by Alessandri of a recurrent tumor of the humerus is an enigma. The lesion was thought from a histologic standpoint to be a mixed thyroid and parathyroid adenocarcinoma. There was no evidence of a tumor in the neck during the eight years that the patient was under observation. This finding seemed important in that it tended to refute the entity of a "benign metastasizing goiter." In an effort to explain the location of the tumor, consideration was given to the possibility that the bone growth might have proceeded from "aberrant embryonic germs" or might have represented cellular elements which were broken away from the mother organ and transported by the blood stream to the bone, where they became manifestly malignant. The author found objections to both of these hypotheses.

FUNCTIONING MALIGNANT PARATHYROID TUMORS

Meyer, Rosi and Ragins in 1939 reported the removal of a tumor of the right parathyroid gland which showed evidence of invasion of the blood and lymphatic channels. There was other cytologic evidence of its malignant nature. The patient had only temporary relief from subjective symptoms of hyperparathyroidism. One year later roentgen therapy was initiated because of a recurrent nodule fixed to the major vessels. Approximately three years from the date of operation death occurred. Necropsy disclosed a recurrent carcinoma of the parathyroid gland, with metastasis to the peritracheal, subclavian and perijugular lymph nodes as well as to the lungs, pleura and right kidney. There was also tumor invasion of the muscles of the thyroid gland and the neck.

In 1937 Petersma reported the case of a parathyroid tumor adherent to the thyroid and the jugular vein. Microscopically it appeared benign except that tumor cells were found within the blood vessels. Postoperatively there was recovery from the signs and symptoms of hyperparathyroidism. One year later there was no evidence of recurrence or metastasis.

Snapper has recorded the case of Gutman. At the time of removal of the parathyroid tumor it was evident that the adjacent thyroid gland was invaded. Microsections disclosed invasion of the blood vessels and the capsule. Clinically the patient improved considerably. However, there was recurrence, and two and a quarter years later several masses were removed which histologically proved to be parathyroid carcinoma. The clinical improvement after the second operation was only moderate. Additional information has been supplied by Dr. Gutman, who writes that the tumor was palpable before operation. Both the original and the recurrent tumor were classified as carcinoma. The patient died about three years after the initial operation.

The case of Sainton and Millot reported in 1933 was that of a parathyroid tumor removed without relief of symptoms of hyperparathyroidism. On reexploration two years later a recurrent tumor was found. Microscopic examination disclosed invasion of the surrounding fatty tissue in some areas.

In 1941 Gentile, Skinner and Ashburn reported the case of a parathyroid tumor which was densely adherent to the left lobe of the thyroid gland and which microscopically showed evidence of invasion of the capsule and blood vessels. After temporary improvement, hyperparathyroidism recurred. Eight months later an enlarged metastatic lymph node on the same side of the neck was excised, as well as another lymph node which showed a vascular space filled with tumor cells. The patient was reported to be in apparently good health without evidence of further involvement three years after the second operation.

Of especial interest is the case of Mason and Warren which was reported in 1931. The authors were undecided as to whether this tumor was an adenocarcinoma of the parathyroid glands or a metastasis to the organs in the neck of an excised carcinoma of the breast which had involved the skeletal system and in one way or the other had resulted in hypercalcemia. The patient gave a history of having undergone a simple mastectomy five years previously for a tumor of the left breast, which was reported to have been a carcinoma. Symptoms suggesting hyperparathyroidism came on gradually over a period of ten months.

On examination there were no nodules in the axillas or the supraclavicular regions. Roentgenograms were interpreted as showing changes compatible with generalized bone metastasis, since there were areas of bone of apparently normal density and structure about the

scattered radiolucent areas which were present in the skull, mandible, scapula, ribs, thoracolumbosacral vertebrae, ilium, right humerus and bones of the right hand including the fourth metacarpal, magnum and unciform bones. (Metastasis of carcinoma to the bones of the hand is a rare occurrence.) The serum calcium was sustained at a high level. The serum phosphorus content was normal. Other laboratory tests disclosed impairment of renal function. Study of calcium intake and excretion over a three day period revealed a negative calcium balance. The patient had had a goiter for "several" years, and the possibility of a parathyroid tumor was considered.

At operation the entire right lobe of the thyroid was occupied by a firm mass 5 cm. in diameter. It was friable and adherent to its bed and to the overlying muscles. Lateral to the upper pole on the right was a flat bean-shaped mass approximately 2 cm. by 1 cm. by 3 mm. It was wax brown and, except for its size, resembled a parathyroid gland. These were excised, as well as a nodule arising apparently from the left lower pole of the thyroid.

Postoperatively, the serum calcium content was lowered but continued to be above a normal level. The serum phosphorus content also came down slightly yet remained within the normal range. The patient recovered slowly from the operation. She died after six weeks at home. Permission for an autopsy was refused.

Tumor tissue removed from the neck was described as being of parathyroid origin. Masses of epithelial cells were present in clusters, occasionally seen in alveolar arrangement. Near the periphery the lymphatic vessels were distended with tumor cells, and there was an invasion of these cells into the perivascular lymphatic vessels of a few of the larger arteries. The thyroid contained an adenomatous nodule, in the wall of which there were clusters of epithelial cells with characteristics similar to those of parathyroid cells. At various points near the capsule of the thyroid gland there was invasion by these tumor cells also. The microscopic diagnosis was adenocarcinoma metastatic to the thyroid and parathyroid glands, probably originating from the breast.

The authors were unable to reconcile the finding of a persistent hypercalcemia with this diagnosis and remarked that if it might result from extensive metastasis to bone they were unable to verify it from their experience or through search of the literature. At the time when this report was made there had been no reported case of an unquestionably malignant tumor of the parathyroid glands which produced hyperparathyroidism, and it was generally believed that malignant tumors of an endocrine gland producing hyperfunction were rare.

Without a more complete knowledge of the tumor it is not possible to say anything definite regarding its source. However, the evidence is suggestive of a malignant hyperfunctioning parathyroid tumor with

secondary skeletal changes. It seems significant that the prominent complaints of the patient in her final illness were apparently more the results of an existing hypercalcemia than of late carcinomatosis.[1]

For further investigation of reported cases of malignant growth of the parathyroid glands and for the sake of completeness, reference is made to other articles listed in the bibliography.[2] Consideration of these cases has not been included since in most instances the material presented leads to indecision and would require lengthy discussion. Often one is aware that the tumor obviously was not of parathyroid origin or was not malignant. The first case of a hyperfunctioning parathyroid tumor which was diagnosed as adenocarcinoma was that reported by Wilder and by Wellbrock in 1929. As brought out, there is doubt that it should be considered malignant.

The list in the accompanying table is not necessarily to be considered as inclusive of all valid reports of carcinoma of the parathyroid glands but represents my opinion based on a study of the material at hand. It is possible also that some of these cases do not belong here (nonfunctioning tumors, cases 5 [Price and Mowatt], 7 [Armstrong] and 2 [Roffo and Landivar]; functioning tumors, case 17 [Young and Emerson]). It is well to emphasize that the great majority of tumors of the parathyroid glands have been benign and surgical removal has been carried out in a conservative manner. Note the frequency with which these tumors were palpable. In the nonfunctioning group, a cervical mass had been present and noticed by the patient for periods of time from two months to thirty-five years and had been reason for medical consultation. The group of patients with functioning tumors sought medical attention for reasons related to hyperparathyroidism. The tumor rarely had been noticed by the patient and was not always recognized on physical examination. The tumors in the patients without hyperparathyroidism were generally much larger than those in the

1. Dr. Shields Warren recently has reviewed the pathologic findings in this case (personal communication) and has come to the conclusion that it is a case of metastatic adenocarcinoma originating in the breast.

2. Since the preparation of this paper, Dr. E. H. Norris has published a collective review on carcinoma of the parathyroid gland (Surg., Gynec. & Obst. **86**:1-21 [Jan.] 1948). He includes a preliminary report of 3 cases which are incorporated in the table accompanying this paper. In his table of cases called parathyroid carcinoma in the literature he lists 41. Of this number, 15 cases were acceptable to him. The 12 cases, excluding the 3 which he records, were reported by the following authors: Meyer, Rosi, and Ragins; Gentile, Skinner and Ashburn; Hall and Chaffin; Toland; Roffo and Landivar; de Quervain; Petersma; Sainton and Millot; McQuillan; Price and Mowatt; Armstrong, and Mendiola. If his 15 cases are accepted and those of Guy and Gutman and the one presented here added, there then are 18 cases which seem to meet the criteria for classification of carcinoma of the parathyroid glands.

Data on Malignant Parathyroid Tumors

Nonfunctioning Tumors

No.	Author and Year	Sex and Age	Palpable Mass in Neck	No. of Operations	Evidence of Recurrence	Autopsy	Histopathologic Nature of Tumor	Invasion or Local Metastasis	Distant Metastasis	Outcome and Comment
1	de Quervain, 1909..	Male 68	Yes (2 mo.)	1	Yes	Yes	Sharply outlined polygonal cells arranged compactly with no tendency to glandular formation; many water-clear cells seen singly and in groups	Lymph nodes	Superior mediastinum; lungs and liver	Death about 8 mo. after operation
2	Roffo and Landivar, 1914	Male 60	Yes (35 yr.)	1	Tumor mass over sternum not removed	Yes	Polygonal cells which varied somewhat in size; arranged in clusters bounded by thin connective tissue partitions	Surrounding connective tissue, thyroid; lymph nodes	Lungs and liver	Death 2 mo. after operation
3	Guy, 1929.....	Female 29	Yes (5 yr.)	3	Yes	No	Chief (predominant) and water-clear cells; original tumor appeared benign; recurrent tumors appeared malignant	Capsule, lymph nodes and blood vessels; several separate cervical masses	Lung?	Evidence of pulmonary metastasis 2½ yr. from first operation; final outcome unknown
4	Toland, 1931.....	Female 60	Yes (8 yr.)	1	No(?)	Not mentioned	"Irregular atypical cells . . . arranged in haphazard fashion"; called adenocarcinoma	"Densely adherent to muscles"	Lung?	Postoperative roentgenotherapy; death 4 mo. after operation, attributed to pulmonary metastasis
5	Price and Mowatt, 1932	Male 49	Yes (8 yr. plus)	2	Yes; Not completely excised	No	"Watery" cells and occasional eosinophilic cell; tumor thought to have arisen from a parathyroid rest	Spread by infiltration involving the skin; regional lymph node metastases	Right thorax and axillary lymph nodes	Postoperative radium and roentgen therapy; death about 9 mo. after second operation
6	Hall and Chaffin, 1934, 1940	Male 46	Yes (5 yr.)	2	Yes	Yes	Chief (predominant) "clear chief" and oxyphilic cells; original tumor appeared benign	Muscles, blood and lymph vessels and lymph nodes; cervical nodules present	Lungs and tracheobronchial lymph nodes	Called malignant adenoma; death 7 yr. after first operation
7	Armstrong, 1938...	Female 71	Yes (4 mo.)	1	No	....	"Large clear chief cells" predominant; tumor was cellular and showed infiltrative properties	Adherent to sternocleidomastoid and slightly so to internal jugular vein; several smaller overlying tumor masses	Mediastinum? (mass present)	Pathologist could not rule out thyroid tumor; apparently well 3 mo. after operation
8	McQuillan, 1938.....	Female 53	Yes (2 yr.)	2	Yes	No	Large clear (predominant) and oxyphilic cells; original tumor appeared benign	Capsule and metastatic cervical nodules; tumor was firmly adherent to trachea	... .	Recurrent nodule 3 mo. after second operation; subsequent course not recorded
9	Mendiola, 1942.....	Female 32	Yes (8 mo.)	1	No	....	Cells appeared malignant and, in general, were arranged in masses separated by connective tissue fibers; epithelial cell columns and cell nests in some places	Capsule not defined; muscle was infiltrated; invasion of blood vessels was a striking feature	No	Postoperative roentgenotherapy; apparently well 3 mo. after operation; area of irradiation was sclerosed

Functioning Tumors

10	Sainton and Milliot, 1933	Male 35	Not mentioned in any report	2	Yes	....	Predominantly eosinophilic cells; adenomatous appearance; recurrent tumor showed malignant changes	Capsule and surrounding fatty tissue	No	No response to roentgenotherapy following first operation; interval between second operation and report too brief to determine final results
11	Petersma, 1937.....	Male 31	Yes (on examination)	1	No	....	Water-clear cells; benign appearance	Vessels; tumor was firmly adherent to thyroid and partially adherent to jugular vein	No	Apparently well 1 yr. after operation (serum calcium and phosphorus were normal)
12	Meyer, Rosi and Ragins, 1939, 1943	Male 56	Yes (on examination)	1	Yes	Yes	Water-clear and transitional cells with cytologic evidence of malignancy; called nonhornifying squamous cell carcinoma	Capsule, blood and lymph vessels and thyroid	Lungs, pleura, lymph nodes and right kidney	No response to roentgenotherapy; death 3 yr. after operation
13	Gentile, Skinner and Ashburn, 1941	Male 38	Yes (recent)	2	Yes	....	Polygonal cells with varying amounts of oxyphilic cytoplasm and with distinct cell borders; recurrent tumor appeared malignant	Capsule, blood vessels and lymph node; original tumor was densely adherent to the thyroid	No	Apparently well 3 yr. after second operation
14	Gutman (from Snapper), 1943	Male 56	Yes	2	Yes	?	Recurrent tumor appeared malignant	Capsule, blood vessels and thyroid	Not mentioned	Improvement following second operation was "only moderate"; death about 3 yr. after first operation
15	Kilgore and Taylor (from Norris), 1947	Female 51	Yes (10 yr.)	1	....	....	Principally large polyhedral chief cells; tendency to form epithelial cords	Capsule, blood vessels, lymph nodes, thyroid and thymus; one of two tumors found was densely adherent to thyroid and to recurrent nerve	No	Patient was recovering from osteitis fibrosa cystica 4 mo. after operation and was still under observation after 1 yr.
16	Ober and Mellman (from Norris), 1947	Male 50	No	3	Yes	....	Original tumor contained polyhedral cells and appeared benign; the cells were larger and more loosely arranged in the subsequently excised tumors	Recurrent tumor showed invasion of connective tissue, muscle and blood vessels; several tumor nodules were removed at the third operation	No	Third operation, about 16 mo. after the first, was radical; serum calcium dropped to 7.7 mg. per 100 cc.; patient was still under observation
17	Young and Emerson (from Norris), 1947	Female 53	No	1	Yes	Yes	Two tumors similar microscopically to those in cases 12 and 15 of this table (Norris)	"Local invasion" (not elaborated on)	No	Serum calcium level was normal for 3 yr. postoperatively, after which it became elevated; death 6 yr. after operation from renal insufficiency
18	Stephenson, 1948...	Male 57	Yes (on examination)	2	Yes	Yes	Chief cells; no cytologic evidence to bear out its malignant nature other than invasion	Capsule, lymph vessels, muscle and thyroid	No	Death followed second operation 2 yr. after first operation; tumor apparently had invaded contiguous structures at the time of first excision
19	Black, 1948.....	Female 53	No	2	Subtotal excision at first operation	....	Classed grade 3 adenocarcinoma by the pathologist (Dr. Broders); chief (?) cells	Infiltration of the muscle; metastasis to regional lymph nodes	No	Postoperative irradiation; outcome awaits time

patients with hyperparathyroidism. The reason is apparent, since a tumor in the locale of the parathyroid glands ordinarily could expand considerably without causing symptoms by its growth alone. The tumor reappeared in the neck after operation in all but five instances. In these the follow-up reports were for one year or less, a relatively short time. As pointed out by Norris, these malignant tumors are notably adherent to contiguous structures.

It is not possible to decide what difference, if any, there might be between the cells of the functioning and of the nonfunctioning tumors. The descriptive terminology of the various authors was often indefinite. This is readily understandable in view of the fact that the types of epithelial cells in the normal adult gland have yet to be adequately classified.

NOTE.—Since the preparation of this paper in its final form, there has appeared another report of a case of adenocarcinoma of parathyroid origin with hyperparathyroidism (Black, B. M., in *Proceedings of the Staff Meetings of the Mayo Clinic,* Jan. 7, 1948). For completeness, this is added to the table (no. 19). The patient had had symptoms of hyperparathyroidism with bone changes since 1944. At the time of the first cervical exploration, in December 1945, a subtotal excision of a parathyroid tumor was carried out. There was improvement for about one year after operation, when symptoms and signs of the disease showed progression. Renal calcinosis also was evident. The second exploration of the neck was performed at the Mayo Clinic in May 1947, and a hard adherent recurrent tumor, along with grossly involved lymph nodes, was removed in a radical manner. There was some evidence of tetany during the early postoperative period, which was controlled by oral administration of calcium lactate. The patient was dismissed three weeks after operation, having received irradiation therapy.

REPORT OF A CASE

E. B., a middle-aged white man, was a patient on two occasions in the Veterans Hospital, Kecoughtan, Va.

First Admission.—On Feb. 8, 1945, the patient fell in his home, injuring the left thigh, and was brought to the hospital in an ambulance. The history was meager. He had been confined to the house for many months because of difficulty in walking. He had sustained a fracture of the right hip "many years ago" and had never completely recovered from it. During the first World War he had been operated on for a dislocated semilunar cartilage of the right knee, which resulted in an instability, for which he wore a brace.

Physical examination disclosed a poorly developed and undernourished man 57 years of age who was confined to bed, the left leg having been put in traction. There was upward tilting of the right greater trochanter associated with tenderness. The right knee was normal except for considerable instability in the extended position. A small mass was palpated on the left side of the neck

anteriorly. The blood pressure was 180 systolic and 100 diastolic (later reading, 150 systolic and 80 diastolic). The pulse rate was regular, 78 per minute. There were no other significant physical findings.

Roentgenograms disclosed a fracture of the left femur 3 cm. distal to the greater trochanter. There also appeared to be a fairly recent fracture of the neck of the right femur. Roentgenograms were made soon after of the skull, chest, pelvis, right upper extremity and right knee. There was an old healed fracture of the right tibia 6 cm. from the knee joint. All bones showed demineralization, and cysts were present in the skull, ribs, right ulna and pelvis. There appeared to be moderate cortical thickening of the parietal bones of the skull. Multiple prostatic calculi were visible.

There was moderate anemia. Smear of the sternal marrow disclosed a normal myelocyte content, with no evidence of plasma cells. Specimens of urine were acid in reaction. The specific gravity ranged between 1.005 and 1.019. Albumin was present on one occasion. A variable number of white and red blood cells and hyaline and granular casts was seen. The serum protein was 7.5 Gm., with albumin 6 and globulin 1.5 Gm. Repeated examination for Bence Jones protein gave negative results.

Other chemical findings, including nonprotein nitrogen, serum calcium and phosphorus contents, are shown in figure 1. The value for serum acid phosphatase was 3. The serum alkaline phosphatase was not determined. (Further studies of renal function were made postoperatively. The phenolsulfonphthalein test showed excretion of 20 per cent of the dye in 2 hours. The concentration test disclosed impaired renal function.)

Because of the initial roentgenographic finding of demineralization of the bone about the fracture site, the possibility of a pathologic condition was apparent, and multiple myeloma or osteitis fibrosa cystica was considered. The diagnosis of hyperparathyroidism was established through the chemical studies of the blood.

The fracture was reduced by traction, and a cast was applied. Calcium was administered orally, and ammonium chloride was given periodically to acidify the urine. The patient's appetite was poor, and he vomited occasionally. On February 27 he passed a urinary stone.

On March 30 the left thyroid region was explored under local anesthesia. Two nodules were present in the region of the left lobe. They were excised, and the wound was closed. One of the nodules, the size of a cherry, was intimately connected with the lower pole and had the appearance of a thyroid adenoma which had undergone degeneration. The pathologist reported it to be a grayish red irregular friable mass measuring 2 cm. in diameter. Section through the specimen disclosed occasional white nodules some of which contained soft yellow areas. The other nodule consisted of a grayish white mass, measuring 0.5 cm. in diameter. It was elongated and flattened behind the thyroid lobe and was thought to be an enlarged parathyroid gland.

On review of the microsections of the tumor, it was seen to consist entirely of chief cells inclosed in a thick fibrous capsule. They were arranged in continuous masses separated by broad bands of wavy collagenous connective tissue. The cells in the centers of the lobulations were larger and stained lighter than those near the stroma. There was some variation in their sizes and shapes adjacent to the fibrous tissue. There were no mitotic figures. The arterioles were markedly thickened. There was no section of normal parathyroid tissue.

From these findings the diagnosis of an adenoma of the parathyroid gland was made.

After the operation when the patient was lifted off the stretcher on to the bed, a pathologic fracture of the right femur 4 cm. from the lesser trochanter was sustained. This was reduced by traction and a cast applied later. Calcium therapy was continued, supplemented by administration of vitamin D. Oliguria or tetany did not develop. His appetite returned, and he showed steady general improvement and gain in weight. By May 2 some increase in the density of the bones was evident roentgenographically. Recalcification progressed rapidly, with disappearance of the smaller cystic areas. Bony union of the fracture sites was complete by the time of his discharge from the hospital on Sept. 29, 1945.

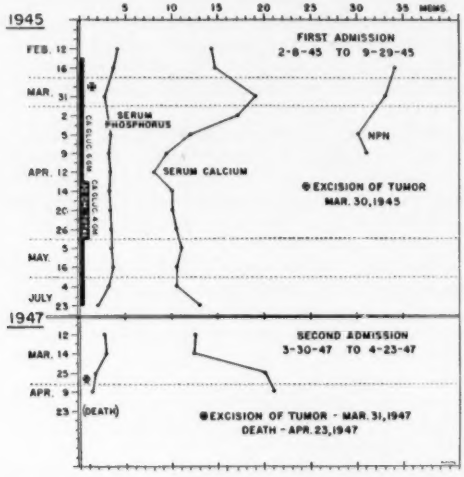

Fig. 1.—Serum calcium and phosphorus values have been charted for the two periods of hospitalization. During the two weeks after the excision of the parathyroid adenoma on March 3, 1945, the serum calcium level dropped from 19 to 8 mg. For the next two and three-quarter months it remained within normal range. Recalcification of the demineralized and cystic bones along with the healing of the pathologic fractures was taken place at a rapid rate and became apparent roentgenographically one month postoperatively. The last chemical analysis, done on July 23, 1945, is significant. The serum calcium level had risen to 13 mg. and the serum phosphorus level, which had remained between 3 and 4 mg., now had fallen to 2 mg. The patient was receiving calcium gluconate during the entire period. The serum nonprotein nitrogen during the first two months was not appreciably increased. After the second admission (approximately sixteen and a half months later) the serum calcium level is seen to rise as the serum phosphorus level falls. Although renal function was not evaluated, the hypophosphatemia mitigates against chronic renal failure. The serum alkaline phosphatase on April 11, 1947 was increased to 11 mg. Severe osteoporotic and cystic changes in the bones had recurred without evidence of pathologic fracture.

Second Admission.—The patient returned to the hospital on March 10, 1947, because of pain in the extremities, weakness, inability to walk and loss of weight. He had had to use the wheel chair to get about at home. The pain and weakness had begun about three months prior to this admission. He also had been constipated for two months, had pain around the heart for six weeks and had frequency of urination and nocturia. He had lost about 40 pounds (18.1 Kg.) in weight during the interval of sixteen and a half months.

Significant findings on physical examination were as follows. The patient was weak and emaciated. He could not speak above a whisper. Laryngoscopy disclosed paralysis of the left vocal cord. An indurated mass the size of a peanut was palpable beneath the operative scar on the left side of the neck. The impulse of the heart could not be felt. There was no apparent cardiac enlargement. The sounds were faint. The rate was regular, 76 per minute. Blood pressure was 170 systolic and 110 diastolic. The right hip was ankylosed, and the muscles of the right thigh were somewhat more atrophied than those on the left. There was no evidence of a fracture. The irregular enlargements of the ribs and right ulna which were observed during the previous period in the hospital had persisted. The abdominal and cremasteric reflexes were absent. The deep reflexes were active and equal.

Roentgenograms were made of the skull, chest, pelvis, femurs, right tibia and right ulna and radius. Generalized osteoporosis was present along with cystic changes in the ribs, left femur and right ulna. There was extensive calcification of the aorta and the iliac and femoral arteries. A stag-horn calculus was seen in the right kidney. The electrocardiogram disclosed left axis deviation.

There was moderately severe anemia. The leukocyte count was 5,650, with 66 per cent neutrophils. One month later the count was 23,300, with 95 per cent neutrophils, at which time the sedimentation rate was 37. Urinalyses showed specific gravities below 1.010, albuminurea and many white blood cells, occasional red blood cells and epithelial cells. The serum alkaline phosphatase was 11. Serum calcium and phosphorus values are shown in figure 1.

On March 31, under local anesthesia, the nodules over the left lobe of the thyroid were excised. The pathologist reported three irregular pieces of tissue, the largest measuring 1 by 1 by 0.5 cm. A study of the microsections disclosed a parathyroid tumor composed of chief cells disposed in broad sheets which were partitioned off by dense connective tissue. The cells as well as their nuclei varied in size and shape. In some places they were small and narrow with hyperchromatic nuclei. In other places they were large and round with pale cytoplasm which showed slight vacuolation. Their nuclei were round and vesicular. Occasionally an eccentrically located nucleolus was seen. There were no mitotic figures.

Adjacent to the tumor mass was dense connective tissue running through striated muscle fibers. Small chief cells with hyperchromatic nuclei were present in groups between some of the muscle fibers.

The patient received symptomatic and supportive treatment. Calcium was not administered. Periodically he experienced pain in the chest and the upper part of the abdomen which required a narcotic for relief. At times he was slightly dyspneic. Facial pain resulted from far advanced pyorrhea associated with the few remaining teeth, which were not extracted because of his poor physical condition. Eighteen hours before his death, on April 23, 1947, his breathing became labored rather suddenly and he lapsed into coma. His tem-

perature had risen from normal to 100 F. during the last three days, with corresponding increase in the pulse rate.

Necropsy.—The body was that of a 59 year old wasted white man measuring 65 inches (165 cm.) in length and weighing approximately 100 pounds (45.4 Kg.). The pupils were round, regular, equal and in mid-dilatation. There was a well healed surgical scar running transversely across the neck.

When the body was opened, the pericardial, pleural and peritoneal surfaces were found to be smooth, glistening and free; each cavity contained a normal amount of transudate. A large abscess filled with thick creamy yellow pus was encountered in the left perinephritic region. It extended under the liver and along the anterior surface of the pancreas, completely filling the lesser peritoneal sac. Within the abscess there were numerous loculated cavities, a smear from which disclosed gram-positive diplococci.

The liver weighed 1,800 Gm. The central areas showed some congestion, with early degeneration of the parenchymal cells. The portal areas were moderately infiltrated with round cells. A small adenoma about 2 mm. in diameter was present just under the capsule. It consisted of branching tubules of low epithelial cells in connective tissue stroma which contained round cells. The epithelial cells had none of the characteristics of parathyroid cells.

The pancreas was indurated. Some purulent exudate was found within its substance. There was extensive interstitial fibrosis which separated the epithelial cells into small islands.

The hilus of the spleen formed part of the abscess wall. There was considerable depletion of the lymphoid cells in the follicles.

The gastrointestinal tract showed no pathologic changes other than some involvement of the esophagus and duodenum by the abscess.

The right kidney weighed 280 Gm. and the left 320 Gm. The right one was normal in size and shape. Its capsule stripped with ease from a smooth surface. A stag-horn calculus was present in the renal pelvis. The relation of cortex to medulla was normal. The left kidney was surrounded by the abscess. Its capsule was densely adherent. The pelvis was distended with purulent exudate. Microsections of both kidneys disclosed numerous calcareous deposits in the collecting tubules and interstitial tissue. There was diffuse fibrosis of the cortex and medulla which was associated with atrophied tubules and areas of dilated tubules. There were many hyalinized glomeruli. Bowman's capsule was moderately thickened. In the left kidney many of the tubules contained pus casts, and there were scattered small abscesses. The arterioles were sclerotic. The adrenals were not unusual.

The urinary bladder contained about 300 cc. of purulent urine, and the trigone was inflamed, especially on the left. The prostate gland was not enlarged. Several calculi and a few minute abscesses were present within its substance.

The heart weighed 400 Gm. On the anterior cusp of the aortic valve was a mycotic vegetation measuring 1.5 cm. The coronary arteries were considerably calcified, which caused diminution of their lumens. The myocardium showed fragmentation with moderate interfibrillar fibrosis. The aorta and its major branches were extensively calcified.

The right lung weighed 1,020 Gm. and the left 820 Gm. They were boggy, with pink frothy fluid exuding from the cut surfaces. In some areas the alveoli were filled with serous exudate and in other areas with purulent exudate. There were no calcium deposits. The mediastinal glands were not enlarged.

The brain weighed 1,320 Gm. There was thick purulent exudate over the vertex, obscuring the convolutions and spreading to a lesser degree over the anterior surface of the midbrain and medulla. The arteries were sclerotic. On section, no gross pathologic changes were seen in the brain substance. The pituitary gland showed some infiltration of basophilic cells, but was not remarkable otherwise.

Fusiform cystic swellings were present in many of the ribs. Microsection of one disclosed the marrow to be almost completely replaced by loose connective tissue. There was thinning of the bony trabeculae, which had disappeared in the most involved areas. A few osteoclasts were seen bordering some of the trabeculae. Osteoblasts were not observed. Hemosiderin was deposited in the periosteum and to a lesser extent in the marrow.

The organs of the neck had been removed en masse. The left thyroid lobe was densely adherent to the ribbon muscles. A parathyroid tumor was located against the trachea posterior to the lower half of the left lobe. It measured 3.25 by 2.25 by 1.5 cm. It was hard, thinly encapsulated and firmly attached by connective tissue. Cut section showed fine lobulations. The left recurrent laryngeal nerve entered the tumor at its lower pole. There was a continuous deposit of tumor tissue along the posterior margin of the left lobe of the thyroid from the inferior to the superior pole. Cut section of the thyroid disclosed the adherent tumor tissue to be well delineated, to penetrate 0.5 cm. in depth and to spread 1.25 cm. over the surface of the gland. An isolated nodule of tumor was seen in the substance of the thyroid 0.2 cm. from the posterior surface. There were also small nodular deposits on the lateral surface of the left lobe just under the capsule. The tumor was light yellow in contrast to the darker tan shade of the thyroid (in the fixed specimen).

A normal-appearing parathyroid gland was found attached to the capsule of the right thyroid lobe at the inferior pole. It measured 8 by 3 by 1 mm.

There were many small hard lymph nodes in the lower third of the neck which showed anthracosis on section.

A review of the microsections made from specimens taken from the neck disclosed little more with respect to the tumor. In one area the chief cells were arranged to form acini which contained colloid-like material. None of the lymph nodes was invaded. However, an encapsulated mass of chief cells was found to be attached to a lymph node, and nests of well differentiated tumor cells were seen in lymphatic channels in the connective tissue stroma. There were also sections of two parathyroid glands. One was oblong. The chief cells assumed an anastomosing cordlike pattern, with an occasional small acinus. There were two large circumscribed islands of oxyphil cells, some of which contained vacuoles. A few scattered fat cells were present. The other section of a parathyroid gland was round. The chief cells were small, and some were arranged to form small acini. There were a few small islands of oxyphil cells. A moderate number of fat cells were present.

The essential diagnosis, including necropsy findings, was (1) postoperative recurrent malignant adenoma of the parathyroid glands, with hyperparathyroidism, manifested by osteitis fibrosa cystica generalisata, nephrocalcinosis, nephrolithiasis, nephrosclerosis and paralysis of the left recurrent laryngeal nerve; (2) left perirenal abscess, with extension, pyelonephritis on the left side, acute, purulent leptomeningitis, acute bacterial endocarditis, involving the aortic valve; (3) severe, generalized arteriosclerosis, and (4) chronic pancreatitis, with marked fibrosis.

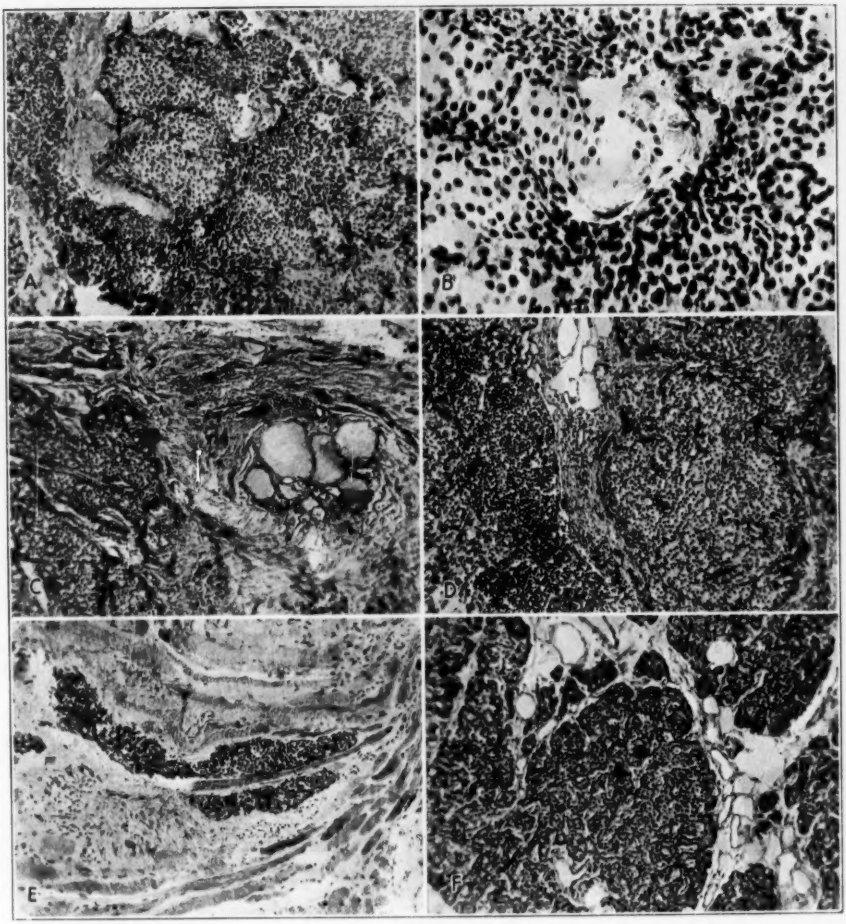

Fig. 2.—*A*, the parathyroid tumor consists entirely of chief cells which are disposed in broad sheets separated by dense bands of connective tissue. In general, the more central cells were larger or stained lighter than those near the stroma. *B*, the parathyroid tumor (higher magnification). The cells as well as their nuclei vary somewhat in size and shape. In some of the larger cells there is vacuolation of the cytoplasm, and a few eccentrically located nucleoli are present. Apparently these are the secreting cells. There are no mitotic figures. *C*, parathyroid tumor in thyroid. *D*, parathyroid tumor in lymph tissue. *E*, parathyroid tumor between prethyroid muscle fibers. *F*, opposite normal parathyroid gland. There is no fat replacement or evidence of "atrophy of disuse."

COMMENT

Only two microsections of the original tumor in this case were available for study, and these showed little or no cytologic evidence which would suggest its inherently malignant nature. Biopsy of the recurrent tumor disclosed invasion of the prethyroid muscles. There was little apparent change in the chief cells. On postmortem examination, the tumor was seen to have spread over the surface of the thyroid and a small nodular area was found within the thyroid substance. The adjacent lymphatic vessels contained tumor cells. The manner in which the tumor had incorporated the left recurrent laryngeal nerve, having produced paralysis of the vocal cord, was further evidence of its malignant disposition. There was no remote metastasis. The remaining parathyroid glands appeared normal for the age of the patient.

The tumor was clinically malignant in that it invaded the contiguous structures of the neck, including the muscles, lymphatic vessels and thyroid gland. Although the surgeon (Dr. Ernest S. Roberts) felt that he had removed all the primary growth, the tumor recurred. The cells and their arrangement displayed no changes to suggest that it was an adenocarcinoma. It was felt that it represented an adenoma which showed invasive character, in other words, an adenoma malignum.

The observation of Guy that apparently benign tumors with a duration of years might take on malignant characteristics seems applicable to parathyroid tumors. The fact that the great majority of the hyperfunctioning adenomas with evidence from the history of long duration which have been removed resulted in recovery from hyperparathyroidism suggests that this seldom does occur. However, in instances in which there has been recurrence, invasion or metastasis, the cytologic appearance has been in no way consistent with the apparent degree of malignancy. When there has evidently been incomplete excision of the primary growth, the recurrent tumor has tended to show a less typical cytologic appearance. There is little doubt that the nonfunctioning malignant tumors of the parathyroid glands reported in the earlier literature in many instances represented carcinoma of the thyroid with metastasis.

It is concluded, therefore, that significant evidence of the malignant character of a parathyroid tumor lies not so much in the cellular picture but rather in evidence of invasion by the tumor cells of the capsule or the lymphatic or blood channels. In some instances it is possible that tumor cells have become incorporated in the proliferating connective tissue barrier of the capsule and do not represent an actual invasion. So it is true that these cells might become displaced as a result of incomplete excision of the tumor.

The stress laid on the necessity of complete removal of parathyroid neoplasms is wholly appreciated (Alexander and others). Incomplete removal with the uncertainty which it entails makes complete extirpation of this type of tumor the only procedure in treatment. This is especially true when the new growth is adherent and should imply removal of the adjoining thyroid lobe as well. Methods of control of the postoperative hypocalcemia have become fairly reliable.

That the size and weight of a hyperfunctioning tumor of the parathyroid glands is significantly important cannot be appreciated. Its capacity to produce hyperparathyroidism would depend necessarily on the number and activity of the cells capable of secreting parathyroid hormone which it contained. It is not fully understood yet which type of cell has this capacity. Apparently the chief cells are the functioning element in the normal state. They represent the total mass of epithelial cells at birth and during childhood. They are involved in adenomas which produce hyperparathyroidism. They also may be the predominant cells in nonfunctioning adenomas. They become hyperplastic in secondary hyperparathyroid states. The darker-staining cytoplasm of the chief cells may represent the hormone in an inactive form.

The nonstaining fluid in the water-clear cells (which shows as vacuolation with increase in volume of the cytoplasmic mass) may represent the activated principle. Stimulus for the delivery of the hormone into the circulation is appreciated in secondary hyperparathyroidism, but there is yet no real clue to the cause of hyperfunction in primary hyperplasia. It appears that the water-clear cell is a form of the chief cell. Since hyperparathyroidism is present in primary hyperplasia, the water-clear cells must function, since they represent the total epithelial substance of the affected parathyroid glands. It has become evident that tumors which consist primarily of oxyphil cells do not produce hyperparathyroidism although there have been reports to the contrary. These cells normally appear after puberty, and whether or not they have a function is not known. What relation these histologically different cells may have to one another needs clarification. It has been stated that the type of cell predominating in a tumor does not appear to affect the clinical course (Alexander and others). Until there is a better knowledge of the cellular physiology of this endocrine organ one hesitates, therefore, to classify these tumors in a manner according to histologic observations.

SUMMARY

An analysis has been made of cases of malignant tumors of the parathyroid glands cited in the literature. The incidence is distinctly rare as compared with that of adenomas, and in many reports of cases of malignant parathyroid tumors the data presented have not been sufficient

or have been inconclusive. The malignant character of the tumor appears to lie not so much in the cytologic picture but rather in evidence of invasion by the tumor cells of the capsule and the lymphatic and blood channnels. It is their nature to manifest themselves first by invasion of contiguous structures. Remote metastasis occurs most often to the lungs and is usually late.

A case of a hyperfunctioning malignant parathyroid tumor, with comments, has been presented. In spite of little cytologic evidence of its malignant nature (excluding invasion and local metastasis) this tumor should properly be called an adenocarcinoma, for no better reason than to impress the need of radical extirpation in such cases as this if a cure is to be one's objective.

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SURGICAL MANAGEMENT OF GASTRIC ULCER HIGH ON THE LESSER CURVATURE

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GASTRIC ulcer at or above the reentrant angle has always posed a difficult technical problem to the surgeon. The many operative procedures described for treatment of these lesions may be divided into two groups: those that leave the ulcer in situ and those designed to remove the ulcer.

For the first group gastroenterostomy and pyloroplasty have been tried and found unsatisfactory for the reason that they are physiologically poor operations which do not attack and remove the acid-bearing and hormone-secreting areas of the stomach. All writers on vagotomy caution against the dangers of supradiaphragmatic vagotomy for gastric ulcer. According to Colp, infradiaphragmatic vagotomy for ulcer with edema and induration reaching the esophagus is a technically hazardous procedure. He advocated a subtotal palliative gastrectomy that leaves the ulcer in situ.[1] Although physiologically this is a sound procedure since it produces achlorhydria and healing of the ulcer, it is open to the objection that an early carcinoma or an ulcer in which carcinomatous change has developed may be left behind. Occasionally it is impossible for the surgeon to differentiate between a benign and an early malignant lesion. If one argues that the end result of resection of malignant lesions is poor at best and that a rare error in diagnosis therefore is statistically not of serious moment, there remains, however, the duty of prognosis that the surgeon owes his patient.

The second group of operations for an ulcer high on the lesser curvature are designed to remove the ulcer. Simple excision, sleeve resections and resection of the lesser curvature, although they fulfil the desirability of removing the ulcer, are poor operations physiologically for the same reasons as gastroenterostomy. The surgical procedure will be followed by a large percentage of recurrences.

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1. Colp, R., and Druckerman, L. J.: S. Clin. North America, **27**:231, 1947.

Total gastrectomy, a sound operation for carcinoma or carcinomatous ulcer, is a formidable procedure, with a mortality rate of 10 per cent in the large clinics. Moreover, postoperative digestive difficulties, inability to gain weight and anemia are not infrequent sequelae of total gastrectomy.

The ideal operation is therefore one that fulfils the criteria of adequate subtotal gastrectomy, permits the retention of a pouch of stomach and removes the ulcer for examination by the pathologist. Zukschwerdt and Horstmann [2] recorded a form of gastrectomy which is designed to fulfil these criteria. The entire lesser curvature is removed and then reconstructed by rotating the greater curvature anteriorly so that the

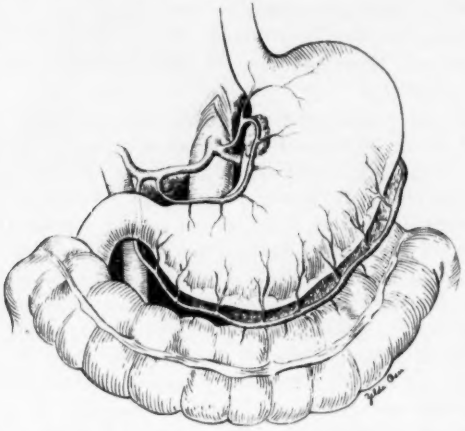

Fig. 1.—Position of ulcer high on the lesser curvature.

suture line becomes S shaped, starting at the cardia anteriorly and ending posteriorly at the opened end of the stomach. Eleven years ago the senior author, faced with an ulcer of the lesser curvature at the cardia, performed for the first time the operation herein described. Since that time, a total of thirteen such operations has been performed.

Until the past year, the left paramedian incision from the xiphoid to the umbilicus was used. Since that time we have used, for these and all other gastric resections, an incision in the upper abdominal area, beginning at the costal margin on the left opposite the eighth interspace. This is carried downward and to the right in a gentle

2. Zukschwerdt, L., and Horstmann, H.: Ergeb. d. Chir. u. Orthop. **29**:440. 1936.

curve as far as a point at the linea alba, half way between the xiphoid and the umbilicus. The incision is then carried in a transverse direction to a point 1 to 2 inches (2.54 to 5.08 cm.) beyond the lateral border of the right rectus muscle. Both rectus muscles are transected. The incision is directly over the stomach in its long axis. Additional exposure for a difficult duodenum may be obtained by continuing the

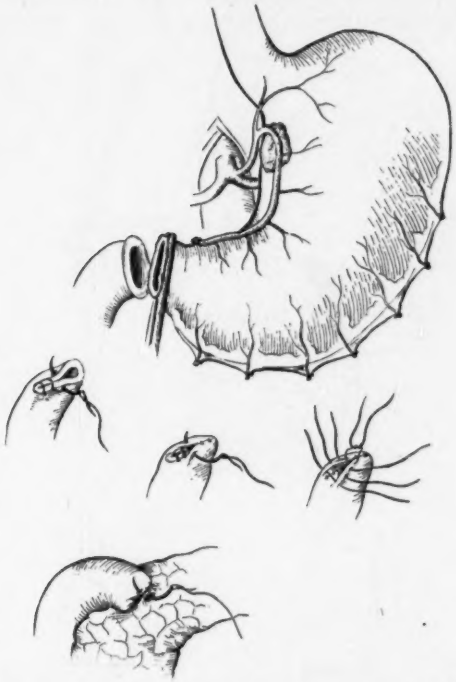

Fig. 2.—Gastrocolic omentum freed and duodenum transected; technic of closure of the duodenal stump.

incision to the right, and further exposure if necessary for high-lying lesions or total gastrectomy may be obtained by cutting through the costal margin at the left extremity of the incision. If desired, the incision may then be carried up the left eighth intercostal space.

Figure 1 illustrates the position of the juxtaesophageal ulcer on the lesser curvature. The resection is begun by transecting the gastrocolic omentum. The pylorus and the first portion of the duodenum are then

mobilized by securing the right gastric and the superior and inferior pancreaticoduodenal arteries. Unless there is an associated duodenal ulcer, this part of the dissection is easily accomplished. A Kocher clamp is placed on the duodenum just distal to the pylorus and the duodenum transected (fig. 2). Crushing clamps are not placed on the duodenum that is to be closed. Figure 2 illustrates the technic of

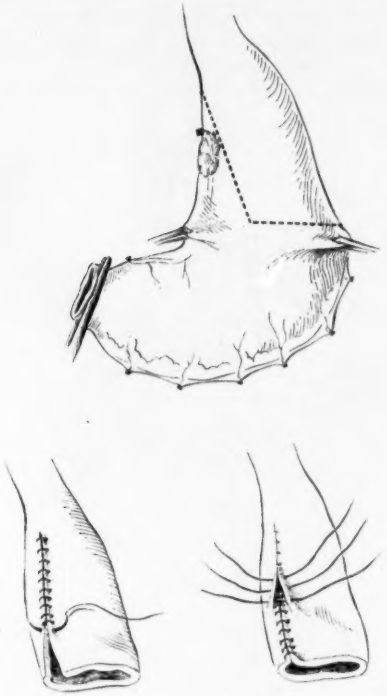

Fig. 3.—Lesser curvature and greater curvature mobilized. Line of transection of stomach shown. Technic of repair of gastric pouch.

duodenal closure which is accomplished with four layers of interrupted cotton sutures.

In figure 3 the greater curvature has been freed beyond the entrance of the short gastric vessels along the gastrolienal ligament. The lesser curvature is then freed as far as the esophagus. The left gastric artery may be secured as it emerges from the celiac axis. Figure 3 illustrates the line of transection of the stomach. This is done between

Kocher clamps. If one desires not to leave crushed stomach behind, Kocher clamps may be applied to the specimen and the vessels in the remaining pouch of stomach may be individually ligated where they project beneath the mucosa.

Figure 3 also illustrates the reconstruction of the lesser curvature. This is accomplished with two layers of interrupted sutures of cotton. This reconstructed pouch now has the shape of an elongated tube that is continuous with the esophagus. The normal outpocketing of the

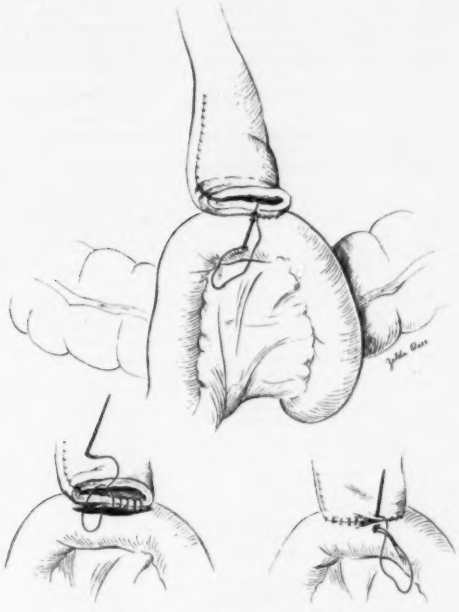

Fig. 4.—Short loop antecolic gastrojejunostomy.

cardiac end of the stomach is no longer present. The redundant tissue is utilized to construct a tube. This is an important step in the procedure and can be accomplished only if the short gastric vessels are previously secured.

An antecolic short loop gastrojejunostomy, with the use of continuous surgical gut sutures, is then performed as shown in figure 4. The abdomen is closed in layers with cotton and without drainage. Postoperatively the Levine tube is left in situ for seventy-two hours. The tube is permitted to drain by gravity. During the first twenty-

four hours, it is irrigated hourly to check its patency. Clear fluids are permitted immediately after operation. Soft, nonresidue foods are allowed after the tube is removed. Thereafter, the diet is rapidly liberalized, and by the ninth day the patient is receiving a full bland

Summary of Reported Cases of Ulcer High on the Lesser Curvature

Patient	Sex	Age	Indications for Surgical Intervention (Along with Failure of Medical Treatment and Question of Malignancy)	Position of Ulcer	Postoperative Course and Comment
J. R.	M	40	Intractable pain	At cardia	Uneventful
J. H.	M	60	Intractable pain, hemorrhage	Above reentrant angle	Uneventful
S. S.	M	45	Intractable pain	Above reentrant angle, ulcer 3 cm. in diameter	Uneventful
N. S.	M	53	Intractable pain, hemorrhage	Close to cardia	Uneventful
E. B.	M	46	Intractable pain, hemorrhage	Ulcer 4 cm. in diameter, reached esophagus, perforated into pancreas and lesser sac	Died 14 days postoperatively; peritonitis and bronchopneumonia (autopsy)
N. Mc	M	53	Intractable pain	Above reentrant angle	Uneventful
W. M.	M	76	Intractable pain	Above and below reentrant angle; ulcer 5 cm. in diameter	Uneventful
C. M.	M	46	Intractable pain, hemorrhage	Above reentrant angle	Uneventful
G. K.	F	47	Intractable pain	At cardia	Uneventful
A. W.	M	54	Intractable pain, obstruction	Entire lesser curvature to esophagus; ulcer 10 cm. in diameter penetrating into liver and pancreas	Uneventful
W. B.	M	47	Intractable pain, hemorrhage, obstruction	At reentrant angle (3 other small ulcers in prepyloric area)	Uneventful
E. B.	F	42	Intractable pain, hemorrhage	Above reentrant angle; ulcer 4 cm. in diameter	Uneventful; pathologic diagnosis: "early carcinomatous change in a gastric ulcer"
L. P.	F	45	Intractable pain	At reentrant angle	Uneventful

Total: 13 patients, 1 death; mortality, 8.5%.

diet divided into five feedings. Patients are now ambulatory on the first day and are discharged from the hospital in nine to eleven days.

The accompanying table lists the pertinent data regarding the 13 patients reported on. There was 1 fatality in this group from broncho-

pneumonia and peritonitis. The occurrence in case 12 justifies this procedure, for the patient involved, who is alive and well, had an ulcer which showed early carcinomatous change.

We believe that adequate surgical treatment for ulcers high on the lesser curvature should fulfil certain criteria. First, the antrum and a sufficient amount of the stomach must be removed to decrease the free hydrochloric acid to, or near, zero. Secondly, the ulcer must be removed so that the pathologist may have an opportunity to testify to its benign or malignant character. Thirdly, a pouch of stomach, sufficient for postoperative comfort and to obviate the physiologic changes of total gastrectomy, must be left. We suggest that our experience with the 13 cases herein reported fulfils these criteria.

SUMMARY

An operation for surgical treatment of juxtaesophageal ulcers of the lesser curvature is described. Thirteen patients operated on during the past ten years are reported.

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CONTRALATERAL RECURRENT HERNIATED DISKS

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TO DATE little has been written about recurrent herniated disks. Most of the articles written on the subject have dealt with recurrence of the intervertebral disk at the site of former operation or at an interspace above or below the one previously explored.

In a follow-up study of Dandy's group of 843 cases, Lenhard [1] examined 147 patients. Of those examined, 20 patients had been subjected to multiple operations supposedly because of recurrent herniation. Twenty-five of these had concealed disks. The exact site of recurrences was not given. In a series of 1,217 patients operated on at the Mayo Clinic, Love [2] found 47 with recurrent protruded disks. He stated that "when a patient has recurrent nerve root symptoms after removal of a protruded intervertebral disk, usually there is further protrusion of fibrocartilage from the same interspace; rarely, another disk is involved." He expressed the opinion that there is no absolute way to prevent recurrence. Fusions of the fourth and fifth lumbar vertebrae not only do not prevent recurrence but may possibly favor disk protrusion at the third lumbar interspace. He did not mention contralateral recurrence in his group of cases. In an analysis of 90 cases, Peyton and Simmons [3] listed three recurrences. In all 3 patients operated on a second pathologic disk was removed. In 1 case the recurrence was at the same interspace, and in the remaining 2 a different interspace was involved.

Spurling verified a contralateral return of pain due to a recurrent cervical disk at the same interspace on the opposite side. This is the only report which I could find of a contralateral recurrent herniated disk.

Four cases of contralateral recurrence of a herniated disk at the same interspace are reported here. Three of the cases were verified

From Temple University Hospital and Medical School.

1. Lenhard, R. E.: End-Result Study of the Intervertebral Disc, J. Bone & Joint Surg. **29**:425-428, 1947.

2. Love, J. G.: The Disc Factor in Low Back Pain With or Without Sciatica, J. Bone & Joint Surg. **29**:438-446, 1947.

3. Peyton, W. T., and Simmons, D. R.: Herniated Intervertebral Disk: Analysis of Ninety Cases, Arch. Surg. **55**:271-287 (Sept.) 1947.

by operation. A fifth case is reported in which contralateral symptoms due to a herniated disk were relieved by operation on the normal side.

CASE 1.—R. S., a white man aged 30, in 1943 complained of severe pain low in the back with radiation to the left sciatic region. The pain was accentuated by sneezing and coughing. The left achilles tendon reflex was absent; there was sensory impairment over the lateral aspect of the left foot. In April 1944 an air myelogram revealed a lateral defect of the air column at the fifth lumbar interspace on the left side (fig. 1). The spinal fluid protein content was 69 mg. per hundred cubic centimeters. Through a hemilaminectomy exposure on the left side a large ruptured disk was removed at the fifth lumbar interspace. There was complete relief from the pain in the back and the sciatic pain. The patient returned to heavy duty and was symptom free until October 1947. While bending over to release an emergency brake on a truck, he felt a sudden "kink" in his back, with sharp tingling pain

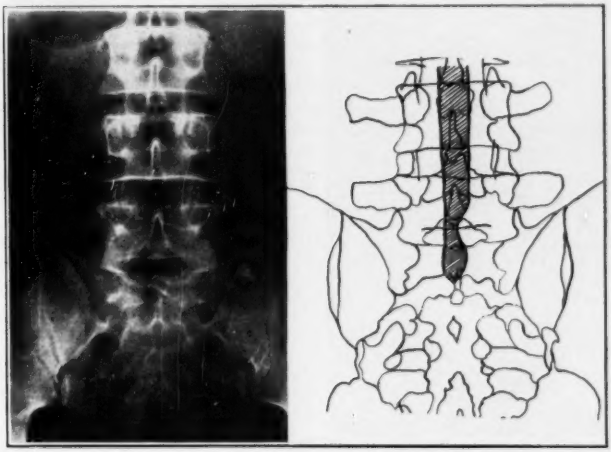

Fig. 1.—Lumbar myelogram showing a defect of the air column (shaded column) at the fifth lumbar interspace on the left side prior to the first laminectomy.

down the back of his right leg into the heel. Reexamination revealed a positive Lasègue sign on the right side. The achilles reflex was unobtainable on both sides, and sensory impairment was found over the lateral aspect of the right foot. A myelogram revealed marked protrusion of the intervertebral disk at the fifth lumbar interspace on the right side (fig. 2). The spinal fluid protein content was 100 mg. per hundred cubic centimeters. On Dec. 17, 1947, a reexploratory laminectomy revealed a large herniated disk at the fifth lumbar interspace on the right side. This was removed. The patient was discharged free of pain and to date has had no further disability.

Comment.—A contralateral recurrence at the same interspace occurred after an interval of three and one half years as a result of a typical form of trauma. Apparently all the herniated material had not been removed at the first operation. The formation of a dense scar at the site of the first removal may have prevented

a secondary herniation on the same side. At the time of the second trauma, a herniation was thus favored contralaterally.

CASE 2.—A white man, a furniture lifter aged 45, complained of pain low in the back for many years. In November 1945 he had, without apparent antecedent trauma, a severe attack of pain in the left sciatic region which persisted for four weeks. There was no pain on the right side. Sneezing and coughing would aggravate the pain. The lumbar region of the spine was rigid and fixed. The left achilles reflex was diminished when compared with the right one. There were no sensory disturbances. The spinal fluid protein content was 58 mg. per hundred cubic centimeters. Air myelography verified the presence of a herniated disk at the fourth lumbar interspace on the left side. On Jan. 18, 1946, a lumbar laminectomy disclosed a massive herniated disk at the fourth lumbar interspace on the right side. This was removed. The patient was discharged on January 31 (two

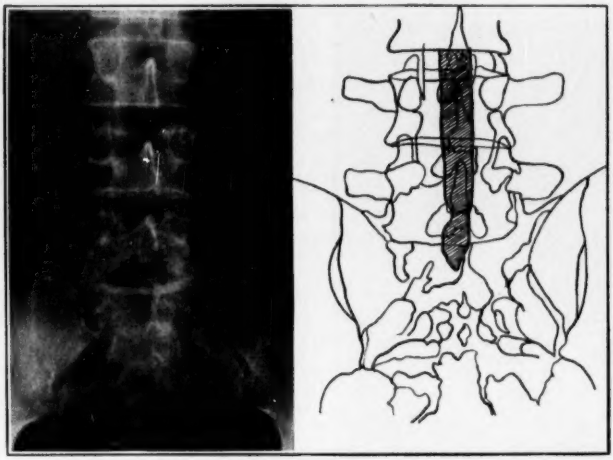

Fig. 2.—Lumbar myelogram showing a lateral defect of the air column (shaded column) at the fifth lumbar interspace due to recurrence of the disk on the contralateral side.

weeks later) free of symptoms. He was readmitted three weeks later because of severe recurrent pain in the back of both lower limbs. On the evening of his discharge he had noted a severe pain in the back which radiated to the lateral aspect of the left foreleg, heel and foot. Two weeks later a similar pain occurred on the right side, while that on the left side had subsided. The pain was not accentuated by sneezing or coughing. The left achilles reflex was absent. There were no sensory disturbances. The spinal fluid protein content was 122 mg. per hundred cubic centimeters. An air myelogram showed a residual space-taking lesion at and slightly above the fourth lumbar interspace. The air column was bilaterally narrowed at this level. On March 2, 1946, a complete lumbar laminectomy was done, with removal of the third, fourth and fifth lumbar laminas. Exposure of the fourth and fifth lumbar interspaces on the left side failed to reveal any protrusion. The dura was opened, and a ventral bulging mass was seen at the fourth lumbar

interspace on the right side. The dura was closed, and a large ruptured disk was removed extradurally on the right side at the fourth lumbar interspace. He was discharged without symptoms and to date has had no pain.

Comment.—This patient had a recurrence of his former pain three weeks after the first laminectomy and then contralateral recurrence five weeks later. A second myelogram disclosed a contralateral recurrent herniated disk which was removed after a complete laminectomy. Perhaps the second laminectomy could have been avoided if a bilateral exploration of the fourth lumbar interspace had been done the first time.

CASE 3.—A 22 year old professional baseball player experienced a sharp pain in the back while pulling a tractor. Five months later sciatic pain developed on the left side. The Lasègue sign was positive on the left, and the left achilles reflex was diminished. An air myelogram disclosed a posterior protrusion at the fourth lumbar interspace, with lateral encroachment of the air column on the left side. A herniated disk was removed at the fourth lumbar interspace on the left side. The protrusion was estimated to measure 1 cm. He was discharged free from pain. Within a few weeks after his discharge, he had a return of sciatic pain, but it was located in the right lower limb. He stated that it was exactly like the former pain on the left side and was located along the same area. Coughing did not accentuate it. Both achilles reflexes were unobtaintable. There were no sensory disturbances. A reexploratory laminectomy disclosed a herniated disk at the fourth lumbar interspace on the right side. When he was discharged two weeks later he had no complaints. At the present time he has returned to his professional duties as a baseball pitcher.

Comment.—Sciatic pain developed on the right side after the removal of a herniated disk at the fourth lumbar interspace on the left side. The recurrence took place within a few weeks after the first laminectomy. Weight bearing would aggravate the pain. As in case 2, a contralateral protrusion may have been present at the first operation. Bilateral exploration at this time, of course, would have answered the problem.

CASE 4.—A 33 year old filling station attendant had pain low in the back of one year's duration without history of trauma. Three months before his admission to the hospital the pain radiated down the back of the left lower limb. The left achilles reflex was diminished. A partially ruptured intervertebral disk was removed at the fourth lumbar interspace on the left side, with complete relief of symptoms. On getting out of bed, he noticed an intermittent pain down the back of the right leg. This pain continued for a period of three months after discharge and then became continuous. Examination at this time failed to reveal any sensory disturbances, but the right achilles reflex was diminished, while the left was active. He planned to be readmitted for operation.

CASE 5.—A 16 year old schoolgirl complained of pain low in the back for three years and then sciatic pain developed on the left side after bicycling. She had been active in all sports. There was a loss of epicritic sensation over the lateral aspect of the left ankle. The achilles reflexes were equal, but the left patellar reflex was diminished in comparison with the right. Pressure over the left paravertebral area caused pain to radiate down the distribution of the left sciatic nerve. A myelogram showed a posterior protrusion at the fifth lumbar interspace. Through a hemilaminectomy exposure on the right side a flattened partially protruded disk was removed on the right side at the fifth lumbar interspace. After operation and to date (one year later) she has been free from all pain. The movements of the lumbar region of the spine are entirely normal, and at present she is actively engaged in sports.

Comment.—The removal of a partially protruded disk contralateral to the side of symptoms and roentgenologic findings resulted in complete abeyance of symptoms. The relief of symptoms on the left side by removal of a disk on the right side suggests that the protrusion on the left side receded after partial removal of its contents on the contralateral side.

COMMENT

One is led to believe from reports in the literature that herniation of a nucleus pulposus occurs unilaterally. However, many neurosurgeons are familiar with the fact that a fair number of patients with ruptured intervertebral disks present bilateral symptoms, which may occur alternately or simultaneously. These symptoms can be explained by the fact that a nucleus pulposus may herniate bilaterally, which results in a dumbell-shaped deformity. I have encountered such deformities on the operating table in patients with bilateral symptoms. In cases in which bilateral symptoms are present a complete laminectomy is advised, with bilateral exposure of the suspected interspace. Some patients may have a midline herniation which may produce bilateral symptoms. In such cases the clinical picture sometimes resembles that of a tumor. The patients are successfully treated by a complete laminectomy, with transdural removal of the midline herniated disk.

With the usual hemilaminectomy approach, complete removal of the disk material is practically impossible. Contralateral recurrent symptoms, therefore, may occur from protrusion of the remainder of the material. In a series of 300 cases contralateral herniation has occurred four times (1.3 per cent).

SUMMARY

Four cases are reported in which contralateral sciatic pain appeared after removal of a ruptured intervertebral disk. The contralateral occurrence was at the same interspace. Three of the 4 cases were verified at operation, and the patients were relieved after exploration of the contralateral side. The fourth patient awaits further surgical intervention. A fifth case is presented in which ipsilateral symptoms were relieved by a contralateral removal of a partially herniated disk. Further reports of such cases may influence the neurosurgeon to perform a more complete laminectomy, with bilateral exploration of the suspected interspace.

TORN DISCOID MENISCUS

Association of Discoid Meniscus with Congenitally High Position of the Fibular Head

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AND
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THE CONGENITALLY HIGH FIBULAR HEAD

The high fibular head is a regressive anomaly resulting from a developmental failure to exclude it from the knee joint.

THE FIBULA IN COMPARATIVE ANATOMY

The five forms of fibular development (Fürst), the urodele, the echidna, the human, the rodent and the ox forms, are shown in figure 1.

The urodeles, such as the salamanders, are tailed amphibia, whose fibula equals the tibia in length. The two bones fuse to form an os cruris in the tailless amphibia (frogs and toads). These are the anura, or the salientia. The fibula articulates with the femur in some reptiles, but the tendency is toward its exclusion. In the turtle there is a slight participation of the fibula in the knee joint. The goose has a fibular facet on the lateral femoral condyle. Herzmark noted that the fibula articulated with the lateral femoral condyle in the alligator and the opossum, the latter lacking the fibular meniscus.

Walmsley discussed the reduction of the mammalian fibula and described three forms:

1. The distal end of the fibula is incorporated with the tibia, as in the existing equidae. The proximal part of the fibula is a stylet-shaped bone bound to the lateral condyle of the tibia. The proximal and distal elements of the fibula are not connected by fibrous tissue.

2. The distal end of the fibula exists as the os malleolare, as in most artiodactyla (even-toed ungulate or hoofed animals). The proximal part of the fibula is a small spur on the lateral condyle of the tibia. The diaphysis in young animals is a ligamentous band passing from the spur to the malleolar bone. The diaphysis is a massive bone in the elephant and a splint of bone in the chevrotain.

3. The distal end of the fibula extends proximally to the protarsal joint in the majority of mammals, as in the monotremes, the marsupials, the carnivores and the primates. The upper end of the fibula is a broad process (peronecranon) on the lateral side of the knee joint for muscles

which move foot and toes. It has its own epiphysis. A second epiphysis is found in the proximal part of the fibula for the surface which articulates with the lateral condyle of the tibia and to a certain extent with the femur. It is connected with the femoral condyle by ligaments.

The fibula is excluded from the knee joint of most mammals, and at the same time a reduction in the rotatory movements of the foot has taken place. The absence of the fibular femoral element allowed the lateral expansion of the tibial condyles. Only in the monotremes and in the scansorial (climbing) and gradatorial (walking) marsupials is it sometimes met with. In general, the proximal extremity of the fibula changes from a pressure epiphysis to a traction epiphysis. The complete absence of the fibula is not seen in any mammalian species, excluding sea-dwelling groups.

The reason for fibular exclusion from the knee joint is the need for associated action of hip and foot joints in the pronograde animal. The

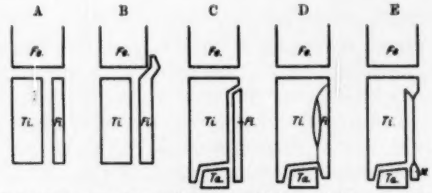

Abb. 1. Schema der Entwicklung und Reduktion der Fibula. A. Urodeltypus. B. Echidnatypus, C. Homotypus, D. Glirestypus, E. Bostypus.
Fe. = Femur. *Ti.* = Tibia. *Fi.* = Fibula. *Ta.* = Talus. *M.* = Os malleolare.

Fig. 1.—The five forms of mammalian fibulas after Fürst. The urodele form is that seen in the tailed amphibia. The echidna form is represented by the monotremes, a low order of mammals. The human form is self explanatory. The word *glires* in the term *glirestypus* is the plural of the latin word *glis*, a dormouse. The "glires" form is the rodent or gnawing animal form. The bostypus is the ox form.

lower end of the fibula becomes the fibula in motion; the upper end is not needed statically and reduces itself to a muscular process.

THE FIBULA IN COMPARATIVE EMBRYOLOGY

Fürst made these observations in ox embryos. An ox embryo of 15.5 mm. showed a relation of tibia, femur and fibula like that in the lower amphibia. The fibula was level with the tibia and touched the femoral condyle. The fibular head curved laterally in an ox embryo of 19 months. The head did not enter the joint in a 25 mm. embryo.

McDermott found that the fibula of the human fetus never articulated with the femur except in that brief time when the tibia and fibula were a single blastemal mass before the formation of the joint space of the knee in the eighth to ninth week of fetal life.

Important are the data on human embryos given to us by Fürst and by Bardeen.[1] The latter found chondrification to begin in the blastema of the femur, tibia and fibula as soon as the outlines of the blastemal skeleton were fairly complete. The tibia and fibula lie directly under the femur from their first appearance as hyaline cartilage.

The 11 mm. Embryo (Bardeen).—The femoral blastema of the embryo was continuous with that of the tibia and fibula distally and with the pelvis proximally. The tibia and fibula were nearly in the same plane. The fibula pointed to the lateral condyle of the femur and the tibia toward its medial one.

The 14 mm. Embryo.—The bones were still indistinctly separated in Bardeen's specimen. Fürst's reconstruction of an equally long human embryo showed good identity of each bone. The tibia was bigger than the fibula. The fibula lay posterior to the tibia and beneath the lateral condyle of the femur. At no point did the fibula touch the tibia.

The 16.5 mm. Embryo (Fürst).—The tibia was separated from the fibula by the thickness of the latter. Both bones lay below the femur, the fibula under the outer side of the lateral condyle of the femur. The tibia had an S-shaped form. Mall noted the temporary distortion of the tibia and fibula by resistance of their ends in a period of rapid growth (embryo of 15 to 20 mm.).

The 20 mm. Embryo.—The three bones were well outlined and the fibula was excluded from the knee joint in Bardeen's embryo. The fibula lay under the lateral femoral condyle in Fürst's embryo of equal length and bent laterally and up to form a processus capituli fibulae.

The 25 mm. Embryo (Fürst).—The fibula was separated from the femur by the laterally expanded tibial condyle and pushed distally. It lay posterior to the tibia, whose proximal end was retroverted. The reduced and not far differentiated fibula reaches its normal position at this primitive stage of development (at 8 weeks).

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1. Mall's table (from Keith) gives the correlation between crown-rump length of the embryo and its age in days or weeks. Part of the table is given.

Crown-Rump Length, Mm.	Age in Weeks
11	6
17	8
25	8
32	9
53	11

The age of any human embryo less than 25 mm. in length is estimated by this rule. The first 5 mm. represent about 35 days of growth and a day of growth is added for each additional millimeter.

Longer Embryos.—The fibular head was not in contact with the femur in the Bardeen embryos 33 and 50 mm. long. The knee joint is formed in embryos between 25 and 30 mm. long.

Developmental Forms of the Human Fibula.—The human fibula as well as the ox fibula passes through the urodele and echidna forms, the ox fibula going beyond the human fibula in reduction. The human fibula is reduced but not greatly differentiated. It holds a rather primitive place in the mammalian series.

Rotation of the Limbs.—The rotation of the limbs is described by Arey. The limb buds appear late in the fourth week as lateral swellings. The upper pair appears first, differentiates earlier and attains its final relative size sooner.

There is no separate note on the time of this rotation or on the behavior of the fibula in rotation of the lower limbs. It has to be carried with the limb which moves from its caudad-pointing position to one at right angles to the body. A ventrad bending then takes place at the knee joint, so that the soles of the feet face the trunk and the great toes are placed on the cephalic border of the limbs. Finally, the limbs turn 90 degrees about their long axis, the lower turning in a direction opposite to the upper. The knee faces ventrad and the sole dorsad, and the tibia is the inner border of the limb. Whether or not this rotation takes place after the extrafemoral position of the fibula is established in the 25 mm. embryo is not given by direct statement.

THE DISKS OF THE KNEE JOINT

In certain reptiles, genuine cartilage plates persist with poor imperforate center. The tibiofemoral meniscus finally splits into two pieces with the progressive displacement of the fibula from the femur. In the higher mammals, both menisci are derived from the partition of the one femorotibial meniscus.

Keith stated that the primitive mammalian knee joint has three disks, the lateral, the medial and the fibular-femoral disk. The primitive mammalian knee joint (fig. 2) shows an articulation of the fibula with the femur. The fibulofemoral intra-articular cartilage becomes included in the tendon of the popliteus muscle.

The external cartilage of the knee is circular in form and continuous with the posterior cruciate ligament in primates. The circular form is lost in man, and it retains only part of its continuity with the posterior cruciate. The external meniscus sometimes persists as a disk, which covers the entire surface of the outer tibial condyle. The internal meniscus is less often discoid.

The giant or discoid meniscus may give no clinical disability. It was first seen by anatomists, such as Young, who noted the anomaly in 1889. Duncan saw a complete lateral disk bilaterally in a Negro dying of pulmonary tuberculosis. We saw it through the arthroscope in each knee joint of a recently deceased man and confirmed this finding when the joint was opened (fig. 3).

Fig. 2.—Scheme of a primitive mammalian knee joint to show (1) the articulation of the fibula with the femur; (2) the fibulofemoral interarticular cartilage which becomes included in the tendon of the popliteus; (3) the tibiofibular muscle out of which the popliteus is evolved; (4) the division of the tibiofemoral interarticular cartilage into external and internal semilunar cartilages. (Keith, from Carl Fürst.)

Fig. 3.—A discoid external meniscus as seen through the arthroscope. The meniscus covered the entire external condyle of the tibia. Its pink inner edge was thicker than any part taken through the body. *1* is the discoid meniscus, *2* the external tibial condyle and *3* the external femoral condyle. (This illustration was published in the *American Journal of Surgery* **43**:501, 1939.)

Owen described a well marked intra-articular septum in 70 per cent of the superior tibiofibular joints examined. It resembled a weak orbicular ligament.

The Variability of the Upper End of the Fibula.—Bennett pointed out the variability of the upper end of the fibula in man. The articular facet may be entirely absent, and the head of the fibula may not reach the tibial condyle.

THE TORN DISCOID MENISCUS IN CHILDHOOD

A small number of papers on discoid meniscus has been published since Kroiss in 1910 pointed out that it is the usual cause of snapping knee in childhood and adolescence. The meniscus is too big for the joint. Middleton reviewed the literature in 1936 and added 4 cases of his own to the 49 reported to that time. Thomson reported 5 more cases in 1946, all involving youngsters between 5 and 13.

Fairbank removed a congenitally abnormal meniscus in 12 of 63 children (13 meniscuses) with internal derangement of the knee. In 9 a discoid meniscus was present. Three lacked the posterior half of the meniscus, and the last had an external meniscus whose concavity faced laterally. The ratio of disability from lesions of the external meniscus to that from lesions of the internal meniscus is higher in children (1.8:1) than in adults (2.3:1). Fairbank saw only 2 cases of an abnormal external meniscus which gave trouble after 20. Were such an abnormality to give symptoms, it would do so before adult life.

CASE 1.—This is an example of a torn discoid meniscus which locked the left knee of a 7 year old girl. The knee had never snapped. It first slipped out of joint in February 1948. A second locking took place on April 9 and a third on April 12, both of which were reduced by Dr. Sidney J. Siegel, who referred the patient. She was examined at the New York Dispensary on April 14. The knees were not locked and had free movement. She ran and walked without limp. Each fibular head was at the level of the knee joint. The left head was loosely bound and its manipulation painful; the right head was firm. The left knee showed slight passive anteroposterior motion and the right none. When the left knee was held bent at 90 degrees, the leg could be turned in internal rotation or pronation of 15 degrees and external rotation or supination of 10 degrees, the motion taking place in the knee. The right knee showed a lesser rotation. The knee was stable in extension.

She had no other obvious congenital anomalies.

The knee locked again on April 19 and this time could not be unlocked by manipulation. A plaster was applied till the child could be operated on. The preoperative diagnosis was (1) torn discoid meniscus with the site of tear presumably at the posterolateral capsular origin and (2) congenitally high fibular heads with laxity of the left superior tibiofibular joint.

The roentgenograms show the high position of the fibular head (fig. 4).

The joint was opened through a median parapatellar incision on May 4, 1948. The ligamentum mucosum was thick, adherent and red; it was resected. The enlarged external fat pad was excised. The external meniscus covered most of the external tibial condyle. Pull on the cartilage disk snapped it forward; it snapped back on release. The disk had torn away from its posterior and lateral capsular insertion and moved forward under the external condyle of the femur to lock the knee. It was not lacerated in its body. The internal meniscus was normal. The fibular head entered the knee. The entire discoid meniscus was removed.

Sections showed degeneration and abnormal vascularization of the meniscus.

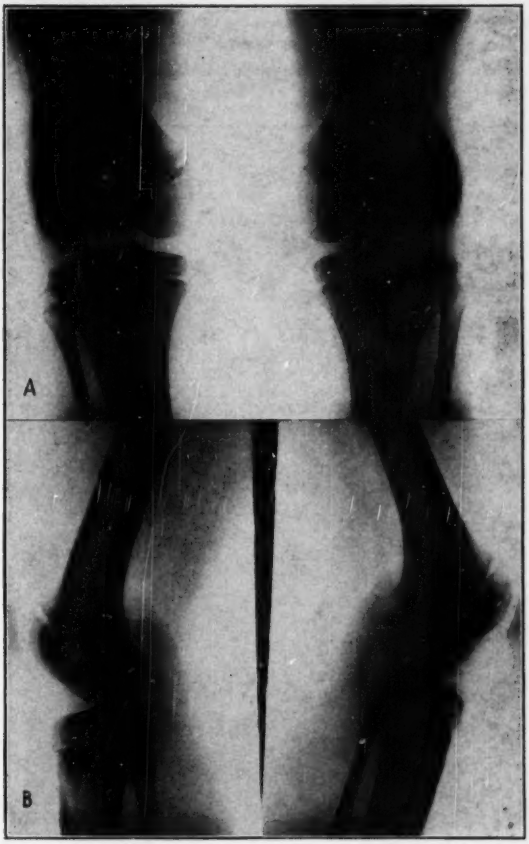

Fig. 4.—*A*, anteroposterior roentgenograms of April 10, 1948. The high position of each fibular head (the urodele form) makes its intrusion into the lateral part of the knee joint inevitable. Each external joint space is wider than the internal, and each external femoral condyle is flattened and less well developed. Each discoid meniscus is visualized as a soft tissue shadow. Careful scrutiny of the left one indicates its heart shape. Its transverse axis has been turned so that it runs from above and medial to below and lateral. The right one, whose axis is transversely placed, is oval, which suggests a full disk. The apex of the left patella is lower than the right. *B*, the lateral views. The superior surface of the left tibia is flat and the crucial eminences poorly indicated. The surface slopes down and forward. The high fibular heads rise above the upper tibial epiphysis.

The patient had no complaints and could walk and run as much and as well as any other child when she was examined on Oct. 15, 1948. The knee extended fully but still lacked 20 degrees of full flexion.

A careful search was made for congenital anomalies on the fibular side of each limb. The fibular heads were high, and the left superior tibiofibular joint now

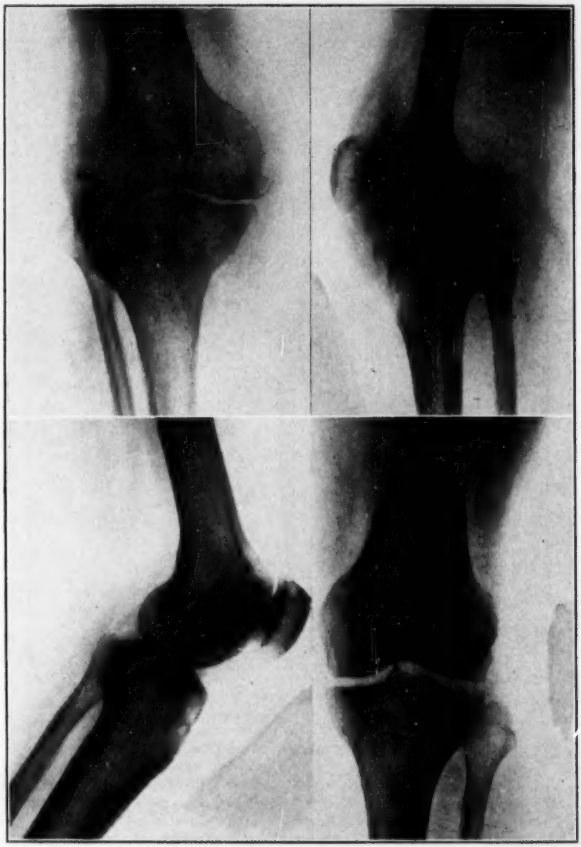

Fig. 5.—Roentgenograms of the high fibular heads in a 55 year old woman. The right knee was the site of pyarthrosis in infancy, so that an unequal rate of growth between tibia and fibula might have given such high fibular position. This premise is wrong, since the fibular head is high in the good left knee.

had little passive motion. The external malleolus of each ankle was more prominent than it should be; the left peroneal tendon—there seemed to be only one—no longer

subluxated over the posterior edge of the external malleolus as it had done when the foot was inverted. Each foot showed two anomalous extensor tendons arising from the most lateral part of the common extensor tendons just below the level of the ankle. One went to the base of the fourth metatarsal bone and could be considered the peroneous tertius. The other, more lateral, tendon ended at the base of the fifth metatarsal bone near its styloid process. It seemed to be an extensor of this bone.

This case is doubly unusual. The discoid meniscus tore and locked the knee joint. It had never caused snapping of the knee, the symptom which enables the diagnosis of discoid meniscus to be made. Locking of the knee joint in childhood should presuppose a congenitally malformed external meniscus, especially if there is another congenital anomaly about the knee.

The high fibular head has never been reported clinically. It is apparently rare. It is likely to be of the urodele form when present. May we assume the presence of a discoid external meniscus when the fibular head is high? The following case (from the Hospital for Joint Diseases, the service of Dr. Leo Mayer and Dr. Henry Milch) may answer the question: High fibular heads were bilaterally present in a woman of 55 (fig. 5). The severely arthritic right knee was locked from joint body incarceration. The shredded and thin external meniscus did not seem discoid when the joint was opened. Arthroscopy of the left knee did show an incomplete external discoid meniscus.

THE TORN DISCOID MENISCUS IN THE ADULT

The literature on discoid meniscus was reviewed in order to find cases like our own in which the discoid meniscus tore and locked the knee. Three groups of cases are recorded: (*a*) cases in which the discoid meniscus without tear is the probable cause of disability, (*b*) the borderline cases in which the condition is between snapping and locking, and (*c*) cases of the locked knee caused by tear of the discoid meniscus.

Group A. The Discoid Meniscus Without Tear.—Ober saw a woman of 31 whose discoid meniscus had neither tear nor split. She had limped since she was 4 or 5 and could never cross her knees. Cave and Staples recorded 7 instances of this anomaly. One of their patients, 19 years old, hurt the knee but did not tear the discoid meniscus. On the other hand, another patient, also 19 years old, had a horizontally split discoid meniscus without injury to the knee. Probably this was a degenerative split, since degenerative changes are often seen in the uninjured or injured meniscus of normal shape (Burman and Sutro). Kulowski and Rickett found a discoid external meniscus whose central and posterior area had been eroded by movements of the knee.

Group B. The Borderline Between Snapping and Locking.—In Finder's case the condition lies in the borderline between the snapping knee and the deranged knee with locking. A girl of 18 wrenched her left knee while dancing. Something in the knee seemed to slip, and presumptive locking of the knee took place, which was reduced by manipulation. The lateral side of the knee was tender and snapped. Operation was done three years later because the knee had slipped out of place at least thirty times. The discoid external meniscus was said to be neither torn nor loose.

Group C. Tear of the Discoid Meniscus Which Locks the Knee.—The preoperative diagnosis is likely to be locking of the knee joint from a torn meniscus. There is nothing to tell that it is a discoid meniscus which is torn unless a story of snapping knee is elicited, which suggests an internal derangement of the knee. Arthrography or arthroscopy may help in the diagnosis. The treatment is the removal of the discoid meniscus.

Dwyer and Taylor reported the case of a 29 year old soldier whose left knee gave way five weeks before when it cracked loudly. This happened several times on the way back to his billet. The knee locked, and extension remained restricted despite splinting of the knee for four weeks. The upper surface of the internal tibial condyle was covered by a discoid internal meniscus. The specimen showed a split in its substance extending from the back end to the front. A horizontal split was seen on its deep surface.

Watson-Jones removed a discoid external meniscus, torn in bucket handle manner near its capsular origin, from the knee of a 16 year old girl who fell playing lacrosse eighteen months before. The knee had always clicked and snapped.

Belcher saw a 19 year old youth in whom the left knee had twisted inwardly with a click a few days before. The knee, as long as he could remember, had always clicked when it was bent from the fully extended position.

The joint was a little swollen with fluid and tender anterolaterally and posteriorly. Internal rotation of the leg was painful. Extension was full. When the knee was bent to 90 degrees, the tibia shook on the femur and the external meniscus moved forward in front of the collateral ligament. A diagnosis of a congenitally abnormal external meniscus had been made, to which the probability of its tear was added when the patient showed no improvement after fourteen days of treatment.

Fifty cubic centimeters of air was introduced into the knee and roentgenograms taken. The medial meniscus was normal. The lateral meniscus showed a line of cleavage in its center, with the major part of

the cartilage extending across the joint by detachment of the meniscus at its medial border. The roentgenograms bespoke a tear of the discoid external meniscus.

It was a little difficult at operation to remove the discoid meniscus from the center of the joint, especially at its anterior end. A well marked tear was seen on the inferior surface of the meniscus which extended up and out but did not reach the upper surface. A niche was seen in the meniscus just behind the tear where the cartilage was not attached to the center of the joint. This seemed to represent an attempt at normal regression of the meniscus.

Four more cases are reported.

CASE 2.—A man, 39 years old, tripped on the cuff of his overalls on April 15, 1942, while going down a stepladder. He fell about 4 feet (122 cm.), landing on his right knee. The knee became painful on its outer side, where he felt something catch.

He had been under observation since 1938, when he injured the same knee in a fall down several steps. The joint was sometimes tender and swollen externally. The knee began to click a little at the end of December 1941. It was not swollen. It could be extended to 175 degrees and bent to 90 degrees. The external joint space was extremely tender. The roentgenograms showed three small opacities in the anterior part of the joint space, possibly osteochondral bodies. There was no high fibular head. A diagnosis of tear of the external meniscus was made.

Arthrotomy was done on June 23, 1942, through a long median parapatellar incision. The ligamentum mucosum was adherent in the intercondyloid fossa. The fat pads were much enlarged but not inflamed. The internal meniscus was normal. The external meniscus was discoid. Traction on the meniscus, after its anterior end was freed by the knife, pulled it forward with a thud because it was torn at its posterior capsular origin. The discoid meniscus measured as much as 2.5 cm. in width at its widest part. Microscopically, it showed degenerative changes, with a tendency to horizontal splitting.

The patient was seen last on Oct. 9, 1942. He tired after walking eight to ten blocks. Extension was 180 degrees and flexion 90 degrees. The joint was neither tender nor swollen.

CASE 3.—A woman, a singer 35 years old, jumped 2 feet (5.08 cm.) from a platform to the stage in a rehearsal at the Metropolitan Opera House on Nov. 12, 1946. The right knee twisted outwardly. It became painful, swollen and locked. She felt as if something were interposed between the joint surfaces blocking extension. She tired when standing and could walk only short distances.

She walked with a limp of the right knee, holding the knee bent. The angle of greatest extension did not exceed 170 degrees; flexion was not limited. The region of the posterior part of the external meniscus was very tender. The roentgenograms of November 23 showed no abnormality. The fibular head was not high. A diagnosis of tear of the posterior part of the external meniscus was made.

The knee remained locked until operation on July 26, 1947. The fat pads were somewhat enlarged but not inflamed. The internal meniscus, a little thinner and narrower than normal, was not torn or loose. The external meniscus was discoid.

Its anterior end was loose, and the meniscus was displaced in part beneath the external femoral condyle and in part into the intercondyloid fossa. When its anterior end was pulled, it moved forward easily and then snapped back into its luxated position when released. The discoid meniscus was removed. Its superior or femoral surface showed a C-shaped imprint; the tibial side was smooth and flat.

Microscopic sections showed a lacerated discoid meniscus.

On Sept. 12, 1947, extension of the knee was 180 degrees and flexion 80 degrees. The patient could not bend the knee easily after it had been extended. She turned the knee out with a little click to make the movement comfortable, a flexion awkwardness due to the space defect left after removal of the disk. Thirty cubic centimeters of an oily yellow synovial fluid was aspirated. She returned to work about October 1.

On October 21, the joint was still swollen with fluid which collected in the joint proper rather than in the quadriceps pouch (separation of the pouch from the joint proper by adhesions). A needle attached to a 5 cc. syringe was inserted into the bulging outer side of the bent joint. The larger syringe with an attached two way stopcock ordinarily used was not available. Twenty cubic centimeters of a clear yellow fluid was aspirated easily. The syringe was removed from the needle as it became full. The plunger of the syringe now seemed to lose its suction power. Another 5 cc. syringe was used. This, too, gave no suction. Air was not introduced into the joint, for the plunger of the syringe was moved back and never forward.

The knee was bent and extended after the aspiration to see if its range of motion was greater. The joint crunched and churned loudly. A roentgenogram showed air in it. Three cubic centimeters of a frothy, bloody fluid was obtained when the joint was again aspirated in the attempt to remove the air. This lessened the crunching. All the air was absorbed three days later, but the joint was warm. The explanation seemed this. The pressure within it was greater than atmospheric pressure when the knee was bent. Air was sucked in each time (four to five times) the syringe was removed to be emptied.

The patient walked with a vague limp on Nov. 20, 1947. The knee was not painful, and she could bend it without turning it out. It was warm. It extended 175 to 180 degrees and flexed 70 degrees.

Case 4.—The left knee joint of a 20 year old girl locked without injury. The knee had snapped for three years. She walked with a limp, and it could not be extended more than 170 degrees but bent fully. A clicking sound was heard on the outer side of the knee on motion, and the region of the anterior horn of the external meniscus was tender.

The roentgenograms showed slight flattening of the external femoral condyle and widening of the external joint space. Both signs are suggestive of a discoid meniscus. The fibular head was not high.

The diagnosis of discoid meniscus or tear of the external meniscus was made. Operation on Aug. 19, 1948, showed a discoid external meniscus which had torn away posteriorly, for it came to lie under the external condyle of the femur when pulled on by a Kocher clamp. A marginal torn piece of the cartilage extended from the anterior attachment of the meniscus to the middle of its lateral portion.

(The patient is being treated on the service of Dr. Harry D. Sonnenschein, Hospital for Joint Diseases, New York. He has been kind enough to allow us to report the case.)

CASE 5.—A 31 year old woman twisted her right knee on Oct. 2, 1948, when she turned in bed. The knee locked and became painful and swollen laterally. It had clicked ever since 1938, when she was struck by an automobile. The right knee could be extended to 170 degrees and flexed to 90 degrees, at which angle a tender, reducible, cartilaginous mass appeared in the region of the external meniscus.

The joint was opened by Dr. Seymour Reissman on October 7. About 30 cc. of a thick yellow synovial fluid escaped. The external meniscus was discoid. Its anterior third was detached near its capsular border. Another laceration, which did not go through the entire body of the meniscus, was seen on its superior surface and its outer middle part. The entire disk, which was 3 to 4 cm. long and 2 to 3 cm. wide, was excised.

The postoperative course was without event.

The preoperative roentgenograms showed a flattening of the external femoral condyle, increased width of the external joint space and a high fibular head of the urodele form.

(Dr. Reissman gave us permission to report this case.)

THE ROENTGENOLOGIC SIGNS OF DISCOID MENISCUS

The roentgenologic signs suggestive of discoid meniscus are the flattening of the external femoral condyle, the widening of the external joint space and the high fibular head. The discoid meniscus itself and its displacement by tear may sometimes be seen.

COMMENT

The tear of the discoid meniscus takes place in the same age groups in which the normally shaped meniscus tears. It is more likely to give way at or near its capsular origin than in its body, since the discoid meniscus is too big for play. The tear is sometimes degenerative. Smillie described the mechanism of the attritional tear as a cleavage by shear.

The history of injury is not always clear, as in the case of Dwyer and Taylor and in case 4 reported here. The case of Finder, probably that of Belcher and case 4 indicate transition from snapping to locking.

Look at the discoid meniscus as one congenital defect in a series of possible defects in the fibular half of the leg. These other defects may be the high fibular head, peroneal tendon luxation at the ankle, probable defect in the fibular muscles, especially the peroneal muscles (failure of separation from the primitive muscle mass), and probable change in shape of the external malleolus. All are defects resulting from failure of normal regression.

The conjoined entity of discoid meniscus and high fibular head is likely to be less common than the entity of discoid meniscus alone.

The discoid external meniscus is a congenital anomaly which may abide symptomless throughout life. It is the common cause of the

snapping knee of childhood and adolescence. It tears, not in its body, but at its anterolateral or posterolateral capsular origin, to give internal derangement of the knee, both in childhood and in adult life.

SUMMARY

Five cases of torn discoid meniscus are reported, as well as the previously unrecorded collateral finding of the congenitally high position of the fibular head. An interesting event in the aspiration of the bent knee, the sucking in of air into the joint, is discussed.

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OSTEOID-OSTEOMA

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IN 1935 JAFFE described a benign tumor of bone which had escaped recognition for a number of years and was frequently misdiagnosed as "sclerosing nonsuppurative osteomyelitis of Garré," "osteomyelitis with annular sequestrum" or "bone abscess," especially when the tumor was present in cortical bone. He defined the neoplasm as follows:

> The lesion is a benign osteogenic tumor of slow growth. The initial phase of its evolution in a given site seems to be the proliferation of the local bone-forming mesenchyme and particularly of its osteoblasts.[1]

Although the neoplasm proper (osteoid-osteoma) measures only about 1 cm. in diameter, the surrounding bone may show considerable thickening (sclerosis).

ETIOLOGY

The etiology of this growth, like that of all other neoplasms, is unknown. Dr. Dallas B. Phemister described the lesion as a localized osteomyelitis of a chronic nature; however, at the present time he has discarded this view.[2] Although a history of trauma may be elicited in some cases, its role as a precipitating factor in this condition has not been established.

In regard to sex and age incidence, the disorder seems to be more common in males and has a predilection for adolescents and young adults, i. e., those in the second and third decades in life. However, cases in which the patients were under 5 and over 40 years of age are on record.

In over 40 per cent of the patients the lesion was in the femur and the tibia. Other skeletal sites are the fibula, calcaneus, talus, tarsal

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After this paper was written, Dr. Sherman reviewed the literature on osteoid-osteoma and reported 30 cases in The Journal of Bone and Joint Surgery, October 1947.

1. Jaffe, H. L.: "Osteoid-Osteoma": Benign Osteoblastic Tumor Composed of Osteoid and Atypical Bone, Arch Surg. **31**:709 (Nov.) 1935.

2. Personal communication to the author.

navicular, patella, skull and facial bones, humerus, ulna, phalanges, vertebra and ilium.

SYMPTOMS

The presenting complaint is usually pain, which is mild and intermittent at first, gradually increases in severity and persistence and often even interferes with sleep. Frequently, the pain is localized to a small area, although at times it may be referred, as in 2 of our cases. It has usually been present for several months or longer and may sometimes antedate any other clinical or even roentgenographic evidence of the disorder. Local swelling may be present if the lesion is in a bone not covered thickly with overlying soft tissue, e. g., the anterior part of the tibia. The presence of a limp or limitation of motion is dependent partially on the proximity of the tumor to a joint surface. A history of fever is never elicited.

On physical examination, localized tenderness is a frequent finding, although 2 of our patients did not show tenderness. Swelling of the soft tissue or bone is discernible in some cases, particularly when the site of the pathologic process is close to the surface, but local heat and redness are absent. However, 1 patient in Jaffe's series had mild elevation of the local temperature, and in 1 of our cases (case 5) there was local redness without elevation of temperature.

The roentgenographic appearance varies somewhat with the site and extent of calcification of the lesion. Early in the course of its development the focal neoplasm appears as a radiolucent area (nidus), tending to be oval in shape when it is in cortical bone and somewhat roundish when it involves spongy bone. On the average its greatest diameter is about 1 cm. Surrounding this nidus (osteoid-osteoma proper) a dense zone of sclerosis varying in size from a few millimeters to several inches may be seen.

This dense perifocal reaction not only extends circumferentially but may extend for a considerable distance above and below the osteoid-osteoma proper if the lesion is in cortical bone.

PATHOLOGIC CHANGES

An osteoid osteoma, as stated previously, is a slowly growing benign tumor of bone arising from the proliferation of osteogenic mesenchyme. Early in the course of its evolution one may see numerous osteoblasts and a few osteoclasts lying in vascular stroma. Eventually the intercellular substance which calcifies slowly and irregularly appears between the osteoblasts, forming patches of osteoid. At a later phase, this osteoid tissue becomes calcified, which gives rise to atypical trabeculae of bone

with intervening vascular intertrabecular tissue which is frequently cellular.[3]

The cause of the perifocal sclerosis is unknown. It consists of hypertrophic irregular compact trabeculae whose marrow spaces are filled with a cellular fibrous tissue and arises from (1) the thickening of original cortical trabeculae and (2) the formation of superiosteal bone.

The clinical laboratory findings from studies which include urinalysis, a Wassermann test, blood count and chemical examination of the blood and cultures at the time of operation are essentially noncontributory to the diagnosis.

TREATMENT

Surgical excision is the only treatment advocated. There is no record of experiences with roentgen ray therapy. Thus far, in all cases reported there has been no history of recurrence when complete excision of the lesion was performed.

REPORT OF CASES

CASE 1.—H. D., a 13 year old white girl, was admitted to the Research and Educational Hospitals in September 1945 because of intermittent dull pain and a mass in the right lower third of the tibia of six to seven months' duration.

A history of febrile episodes or local inflammation was not elicited. Slight trauma to the area may have occurred a year before. The past history was noncontributory. On physical examination, the right lower extremity was slightly atrophic. A nontender hard fusiform mass, about the size of a walnut, connected with the anteromedial aspect of the lower third of the right tibia was visible and palpable. Local heat, edema and redness were absent. Clinical laboratory findings from studies including a Wassermann test, urinalysis, blood count and chemical examination of the blood were normal.

Roentgenograms of the right leg showed a small oval-shaped area of rarefaction in the lower third of the tibia; the cortex on the posteromedial side was thickened and sclerotic (fig. 1 *A*). On Oct. 14, 1945, through an anterior incision, the posterior two thirds of the affected tibia was removed by means of a Gigli saw. A small graft which was taken from the upper end of the right tibia was inserted into the defect.

Microscopically, serial sections of the sclerotic bone (fig. 1 *B*) showed a central nidus of osteoid-osteoma which accounted for the oval-shaped area of rarefaction seen in the roentgenogram. The nidus was found to be composed of irregular trabeculae of partially calcified osteoid, which were lined with osteoblasts. A moderate number of giant cells of the osteoclastic variety were scattered throughout the section. A vascular osteoblastic connective tissue occupied the intertrabecular spaces. The surrounding cortical trabeculae were thickened, and their marrow spaces were filled with cellular fibrous tissue.

3. Jaffe, H. L., and Lichtenstein, L.: Osteoid-Osteoma: Further Experience with This Benign Tumor of Bone, with Special References to Cases Showing Lesions in Relation to Shaft Cortices and Commonly Misclassed as Instances of Sclerosing Non-Suppurative Osteomyelitis or Cortical-Bone Abscess, J. Bone & Joint Surg. **22**:645 (July) 1940.

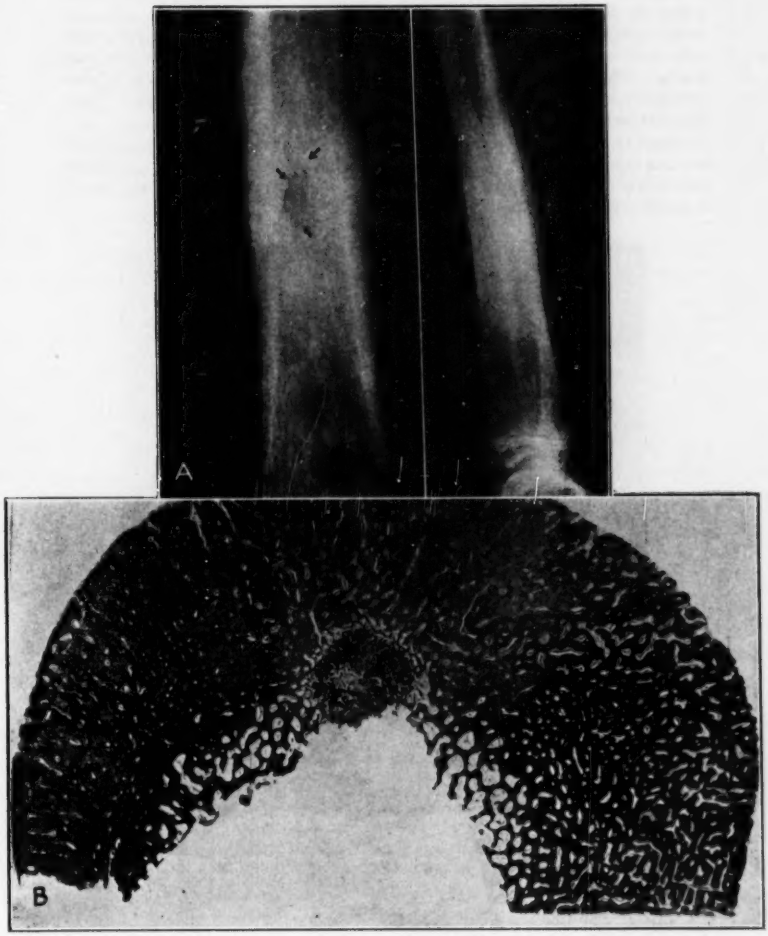

Fig. 1 (case 1).—*A*, roentgenogram of the right tibia. The oval-shaped nidus measures 1 cm. in diameter and is clearly visible in the anteroposterior view as a radiolucent area which is spottily calcified. The lateral view shows the extent of surrounding sclerosis (the radiolucent nidus is not discernible). *B*, photomicrograph of a cross section through the middle of the lesion showing small central nidus of osteoid-osteoma which is spottily calcified. The surrounding cortical trabeculae are hypertrophied.

CASE 2.—The patient was a 7 year old white boy who was referred to the orthopedic dispensary from the pediatric service, because of intermittent sharp pain in the right knee, which seemed to radiate at times up to the lateral aspect of the right thigh. The pain, which was noted six to eight months before his admission, was not related to activity or to changes in weather, nor was it worse at night or relieved by heat. Two months before his admission the patient began to limp. The past history was noncontributory.

Physical examination revealed a well developed, well nourished boy without relevant symptoms except for the suggestion of slight limitation of internal rotation and flexion of the right hip. Tenderness and signs of inflammation were absent. Laboratory findings were normal.

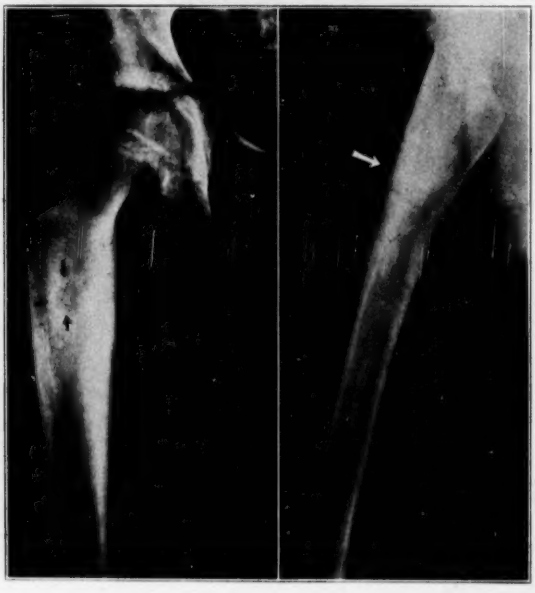

Fig. 2 (case 2).—Roentgenogram of the right femur showing the small radiolucent round nidus. The surrounding density is confined mostly to the anteromedial aspect of the femur. Note the thin plaque of subperiosteal bone deposition on the anterior surface (in the lateral view).

An anteroposterior roentgenogram of the right femur showed a small oval radiolucent area 1 cm. in diameter in the anteromedial aspect of the right femur near the lesser trochanter. In the lateral roentgenogram of the same area a layer of new subperiosteal bone was visible (fig. 2, lateral view).

A clinical diagnosis of osteoid-osteoma was made, and on Dec. 13, 1945, the anteromedial aspect of the affected femur containing the lesion was removed. The defect was filled with bone chips, which were taken from the adjacent cortex of the femur.

On gross examination the specimen measured 5 by 2 by 1.5 cm. A plaque of trabeculated, pitted bone about the size of a half-dollar was present on the cortical surface of the excised fragments. This corresponded to the area of subperiosteal bone which was visible on the lateral roentgenogram.

Microscopically, the sections showed hypertrophic perifocal bone. The plaque of bone described was clearly discernible as a layer of newly added subperiosteal trabeculae which was separated from the main cortical surface by a small amount of fibrous tissue (fig. 3*A*). The nidus was found to be composed of irregular trabeculae of osteoid which were moderately calcified. The stroma consisted of highly vascular osteoblastic tissue. Numerous giant cells of the osteoclastic variety were scattered throughout the intertrabecular spaces, and some were lying in Howship lacunas of the atypical trabeculae (fig. 3*B*).

The wound healed uneventfully. Recent roentgenograms of the femur showed that the defect was replaced by dense bone. Cultures at the time of operation did not show any growth.

CASE 3.—The patient was a 14 year old white boy who was admitted to the Research and Educational Hospitals on April 9, 1946, because of a painful swelling of the left ankle, which had been getting progressively worse. The onset was rather sudden one year prior to his admission. The pain was worse at night and was increased by motion and somewhat by inclement weather. The past history was noncontributory. (There was no history of trauma or of febrile episodes.)

Physical examination revealed loss of contour of the ankle region because of swelling around the joint and in the heel. Eversion of the foot caused exquisite pain. Considerable atrophy of the entire lower extremity was present.

Roentgenograms showed a diffuse area of increased density in the os calcis surrounding a faint radiolucent round area 1 cm. in diameter in the region of the sinus tarsi.

Laminagrams of the os calcis revealed the true nature of the lesion. The center of the nidus was traversed by spotted irregular calcification. A ring of solid density enclosed this center, which in turn was demarcated from the surrounding perifocal sclerosis by a halo of radiolucency about 1 mm. in diameter (fig. 4*A*).

A diagnosis of osteoid-osteoma was made, and on May 2, 1946, the affected area was excised en bloc, including part of the anterior cartilage of the posterior articulating surface of the calcaneus. Arthrodesis of the entire subtalar joint was performed with the aid of an iliac graft.

Microscopic examination of the section through the articular surface and adjacent subchondral bone of the calcaneus showed a circumscribed lesion 1 cm. in diameter which had a characteristic appearance of an osteoid-osteoma. This lesion extended to the under surface of the articular margin, where resorption of the cartilage had taken place.

Some irregular but otherwise not remarkable bone trabeculae surrounding highly vascular and fibrosed marrow spaces were present between the tumor and the joint surface. The tumor itself was somewhat layered, having zones of irregular bone trabeculae encircled by almost solid sheets of osteoid. The whole lesion was extremely vascular; large vessels and thin-walled vascular sinuses led into the substance of the tumor from the fibrosed marrow spaces of the surrounding hypertrophied bone (fig. 4*B*).

CASE 4.—D. A., a 7 year old white girl, was admitted to the Children's Memorial Hospital on Jan. 15, 1940, because of intermittent pain in the right knee of two years' duration. Three months prior to her admission the pain became more severe, particularly at night, and interfered with weight bearing. It usually lasted fifteen

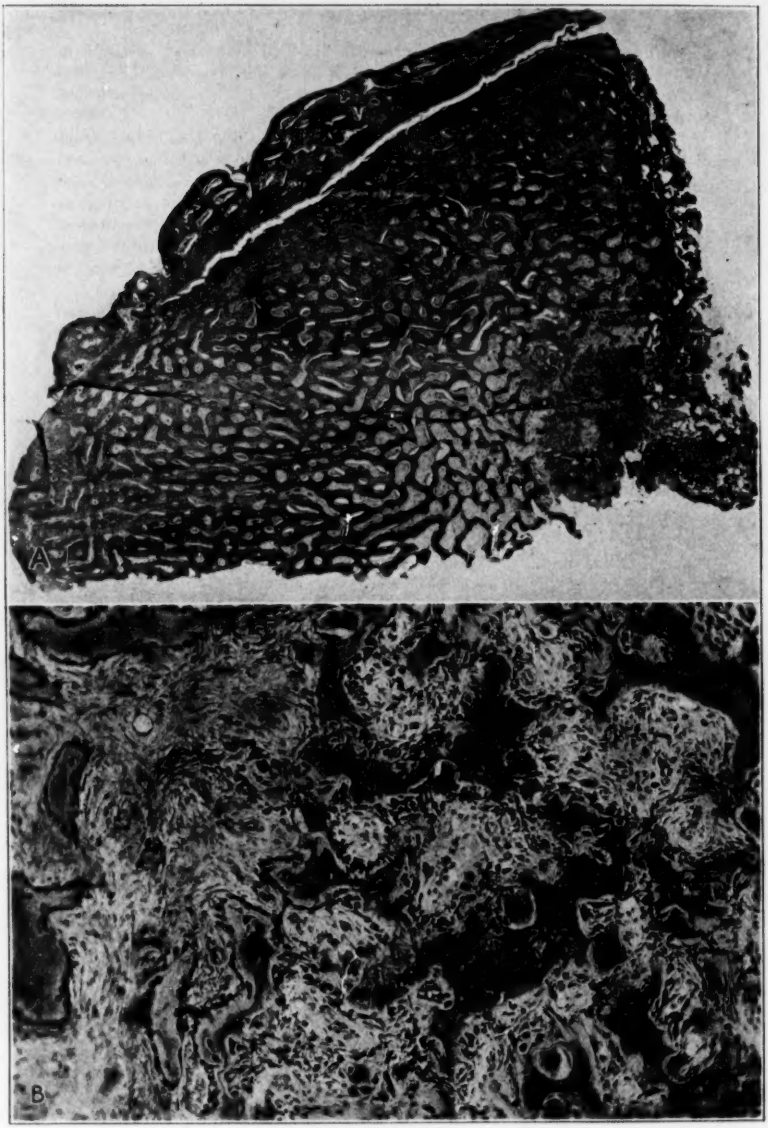

Fig. 3 (case 2).—*A*, photomicrograph of a cross section through the center of the lesion showing the round nidus of osteoid-osteoma. The subperiosteal plaque of bone is partially separated from the hypertrophic original cortex by fibrous tissue. *B*, photomicrograph showing atypical trabeculae, some of which are partially calcified, lying in vascular connective tissue. Note the osteoblasts at the periphery of the trabeculae. Several giant cells (osteoclasts) are visible.

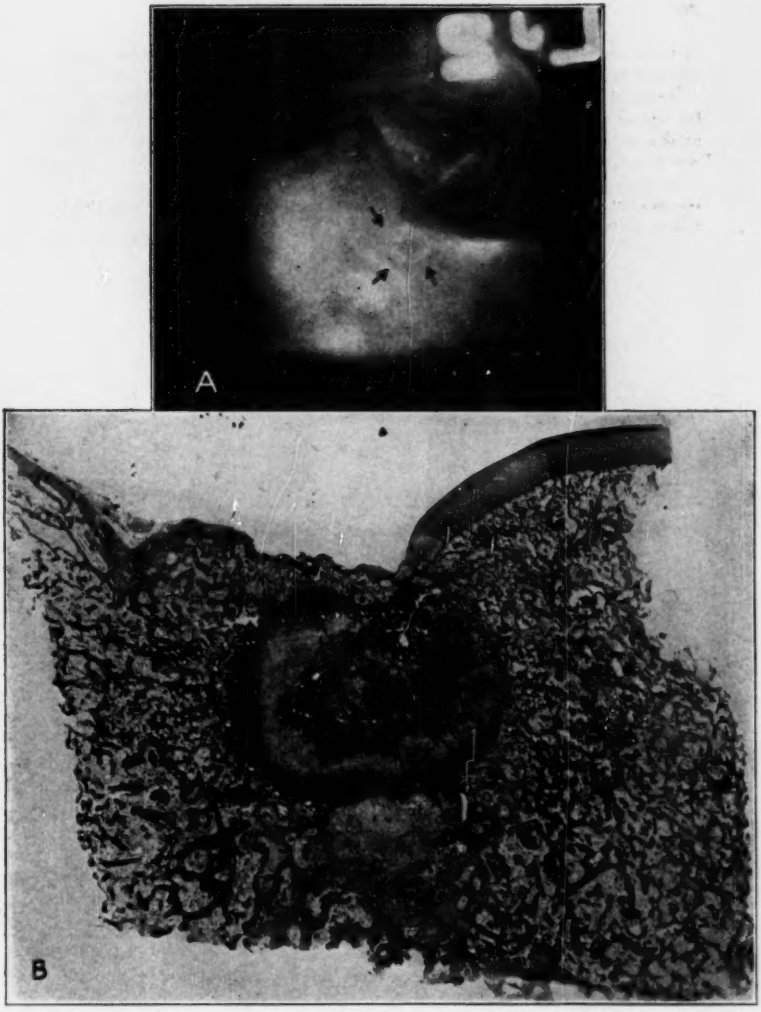

Fig. 4 (case 3).—*A*, lateral laminagram (at 2 cm.) of the left os calcis showing a relatively dense round nidus with a radiolucent periphery situated near the subastragalar joint and sinus tarsi. The surrounding bone in the os calcis is dense (sclerotic). *B*, photomicrograph of a longitudinal section through the center of the tumor showing the partially calcified nidus. Note that the peripheral portion is relatively light (uncalcified or osteoid tissue), which corresponds to the halo of radiolucency present in the roentgenogram.

to thirty minutes. In the interim the patient was normal. The mother called attention to the fact that the child's right foot perspired more than the left.

Physical examination revealed some tenderness in the right inguinal region, but motion of the hip was normal. The right foot was moist and 3 degrees (centigrade) warmer than the left (skin temperature). The skin of the right large toe was macerated.

Roentgenograms of the right hip showed a round zone of radiolucency in the region of the lesser trochanter. Deposition of new subperiosteal bone was clearly visible on the anteromedial side (fig. 5).

Fig. 5 (case 4).—Anteroposterior roentgenogram of right femur showing round radiolucent area in region of lesser trochanter; subperiosteal bone formation is present on the medial side.

The lesion was resected locally, and the defect was filled with chips taken from the surrounding bone.

Microscopic examination of the lesion showed typical osteoid-osteoma (fig. 6 *A*). At the periphery of the nidus several large bundles of nerves were found lying in close proximity to thin-walled blood vessels (fig. 6 *B*). The exact relationship of the nerve bundles to the lesion proper and the symptoms is conjectural. They probably represent sympathetic nerves which normally accompany the blood vessels and account for the vasomotor phenomenon (increased local temperature and sweating of the foot), which was noticed in this case.

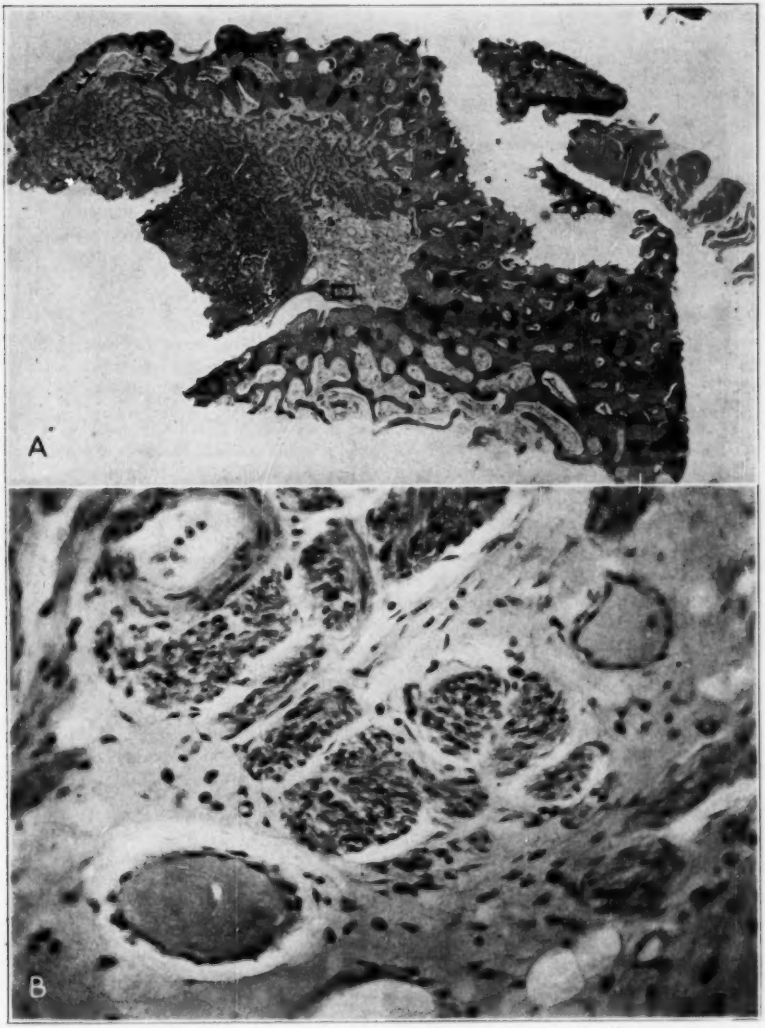

Fig. 6 (case 4).—*A*, photomicrograph of a cross section of the lesion. *B*, high power photomicrograph of rectangular area in *A* showing nerve fibers (probably sympathetic).

After excision of the lesion the temperature of the foot returned to normal within a few weeks.

CASE 5.—H. W., a white boy aged 14 years, was admitted to St. Luke's Hospital under the care of Dr. F. W. Hark because of a painful swelling of the right index finger of two years' duration.

Physical examination revealed a bulbous terminal phalanx which was exquisitely tender and hyperemic. The nail was hypertrophic. Systemic fever and leukocytosis were absent. A tentative diagnosis of hemangioma was made.

Roentgenograms showed the true nature of the lesion. It consisted of a round rarefied zone in the terminal phalanx which contained a relatively dense fragmented area of calcification. At operation the calcified area, which measured 5 mm., was lying free in the rarefied zone; the bed was curetted. Microscopic examination of paraffin sections of the nidus revealed trabeculae of calcified osteoid lying in scanty stroma of connective tissue.

The symptoms subsided after operation, and the bone healed uneventfully.

CASE 6.—D. K., an 11 year old white boy, was admitted to the Children's Memorial Hospital in June 1941 because of pain and swelling in the left tibia of six months' duration. The swelling was noted shortly after the boy was kicked in the leg while playing football. The pain was intermittent and severe enough to awaken the patient at night.

On physical examination the hard swelling in the middle third of the tibia was slightly tender; the overlying skin was freely movable and not inflamed. Fever was absent. The white blood cell count was 12,400. Urinalysis and a Wassermann test gave negative reactions. Roentgenograms revealed a sclerotic area in the middle third of the tibia. A small oval radiolucent nidus was present in the anterior cortex.

A local excision of the lesion was performed. Microscopic examination showed osteoid-osteoma.

CASE 7.—J. M., an 18 year old white boy, was admitted to the orthopedic service on Jan. 15, 1947, because of dull aching pain in the left hip which began shortly after a fall in February 1946. The pain radiated to the left knee and was alleviated by acetylsalicylic acid, but not by heat.

Physical examination revealed an area of "finger point" tenderness posterior to and below the left greater trochanter. External and internal rotation of the left hip was slightly limited. The left thigh was 3 cm. smaller than the right. Roentgenograms showed a small radiolucent area in the posterolateral aspect of the left femur (upper third). The surrounding bone was not markedly sclerotic.

The lesion was excised, and microscopic examination confirmed the clinical diagnosis of osteoid-osteoma.

SUMMARY

Etiologic, pathologic and clinical factors of esteoid-osteoma are reviewed. Seven cases are presented, including 1 case which showed vasomotor changes (increased sweating and a local rise in temperature). These changes were probably caused by stimulation of the sympathetic fibers which were found near the nidus. Pain in osteoid-osteoma may be referred. Laminagrams may be of value in localizing the lesion.

SYMPTOMATOLOGY AND DIAGNOSIS OF GASTRIC CANCER

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GASTRIC cancer is the cause of death in approximately one fourth of all patients who die of cancer. The incidence of resectability in patients with gastric cancer who came to operation at the Memorial Hospital is 39.8 per cent (cardia, 59 per cent).[1] The resectability rate reported in the literature ranges from 25 to 50 per cent.[2] The rate of five year survival without recurrence in patients recovering after operative removal of their gastric cancer is 34.7 per cent at the Memorial Hospital, varying from 42.8 per cent of the patients without nodal metastasis to 24.2 per cent of those whose disease was not confined to the stomach.

This study was undertaken in an attempt to determine whether any correlation existed between the duration and type of symptoms or physical findings and the resectability rate among 1,117 patients with gastric cancer studied and treated at the Memorial Hospital from 1916 to 1946. In the second section of this report the results of gastric analyses, hematologic studies, stool examinations and gastroscopic and roentgenologic findings are considered from the point of view of their diagnostic and prognostic significance.

FREQUENCY OF SYMPTOMS

Chart 1 lists the most common symptoms presented by 1,112 patients with gastric carcinoma. The percentage of patients exhibiting each symptom is indicated by solid, cross-hatched or open bars. The solid bars indicate the percentage of the total number of patients, the cross-hatched bars the percentage of patients whose cancer was considered inoperable and the open bars the percentage of patients whose cancer

From the Gastric Service of the Memorial Hospital.

1. Livingston, E. M., and Pack, G. T.: End-Results in the Treatment of Gastric Cancer, New York, Paul B. Hoeber, Inc., 1939.

2. Pack, G. T., and McNeer, G.: End-Results in the Treatment of Cancer of the Stomach, Surgery **24**:769-778, 1948.

was resected. There were few significant differences in the frequency of each symptom among the three groups of patients, with the exception of dysphagia, which occurred twice as often in patients with inoperable gastric cancer as in patients with resectable cancer. Dysphagia, therefore, would seem to indicate a bad prognosis, yet paradoxically the resectability of cancer of the gastric cardia is 20 per cent greater than that of cancer of the stomach as a whole. Before 1940 cancer of the cardia was inoperable because the technic of cardiectomy had not been perfected. Since dysphagia is more frequent in cancer of the cardia, an undue weight is given to this category. Cancers of the cardia are now likely to show a high percentage of resectability because they apparently often give an early manifestation of their presence in the form of dysphagia.

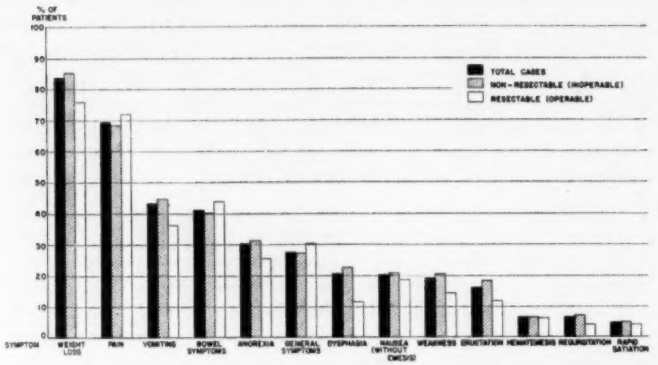

Chart 1.—The most common symptoms presented by 1,112 patients with gastric cancer (886 inoperable and 226 operable cancers). The percentage of patients exhibiting each symptom is indicated by solid, cross-hatched or open bars. The solid bars indicate the percentage of total number of patients, the cross-hatched bars the percentage of patients whose cancer was considered inoperable and the open bars the percentage of patients whose cancer was resected.

In the discussion immediately following, percentages are listed in this order: (1) the total number of patients, (2) patients with inoperable gastric cancer and (3) patients with resectable gastric cancer. The group designation is not repeated each time but is given for the first symptom—loss of weight—as a guide.

Loss of weight, the most frequent of all the symptoms exhibited, occurred in 83.5 per cent (of the total number of patients), 85.4 per cent (of those with inoperable cancer) and 76.1 per cent (of those with resectable cancer); pain in 69.1, 68.3 and 72.1 per cent; vomiting in 43.1, 44.8 and 36.3 per cent; bowel symptoms in 41.1, 40.3 and 44.2

per cent; anorexia in 30.2, 31.4 and 26.9 per cent; general symptoms [3] in 27.6, 27.1 and 30.1 per cent; dysphagia in 20.4, 22.7 and 11.5 per cent; nausea in 20.2, 20.7 and 18.6 per cent; weakness in 19.2, 20.5 and 14.2 per cent; eructation in 17.2, 18.5 and 11.9 per cent; hematemesis in 6.4, 6.4 and 6.2 per cent; regurgitation in 6.4, 7.0 and 4.0 per cent, and rapid satiation in 4.6, 4.7 and 4.0 per cent. There were no symptoms mentioned by 0.4 per cent of the patients.

In chart 2 the degree of weight loss in 10 pound (4.5 Kg.) increments is given for 834 patients with gastric carcinoma. Again, the solid, cross-hatched and open bars are used to indicate the percentage of the total number of patients, the patients with inoperable cancer and patients whose cancer was considered operable exhibiting a given loss of weight. Twelve per cent of the inoperable group and 23 per cent of the operable group had lost 1 to 10 pounds (0.5 to 4.5 Kg.), with the

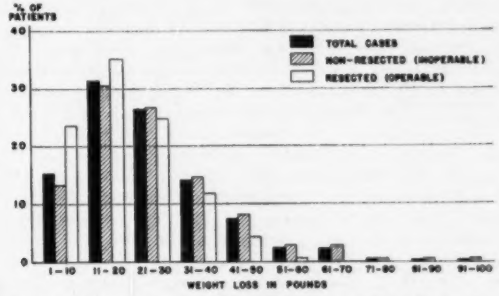

Chart 2.—The degree of weight loss in 10 pound (4.5 Kg.) increments for 834 patients with gastric cancer (672 inoperable and 162 operable cancers).

degree of loss essentially the same in subsequent categories until the 41 to 50 pound (18.6 to 22.7 Kg.) classification, into which fell 8 per cent of the inoperable group and 4 per cent of those whose cancer was resected. Only 1 patient with a loss of weight above 50 pounds (22.7 Kg.) had operable carcinoma.

In the present analysis we do not propose to elaborate on the significance of the various symptoms, but a practical word concerning loss of weight is in order here. In these tables only the absolute loss is recorded. Two factors are of great prognostic significance, namely, the relative loss of weight, i. e., compared with the original weight of the patient, and the rapidity with which the loss occurs. The pound for

3. General symptoms include fatigue, fulness, pyrexia, "stomach consciousness," tenderness, aversion to meat, bad taste and symptoms unrelated to the gastrointestinal tract.

pound loss is less important in an obese patient than in one of hyposthenic habitus. As a rule the more rapidly a loss of weight occurs, the more marked are the hepatic dysfunction, hypoproteinemia, state of inanition and other metabolic deficiencies. For example, the loss of a given amount of weight in six weeks is more serious than if the same loss occurred over six months.

These statistics parallel those reported in the literature,[4] with the incidence of weight loss varying from 56 to 96 per cent, of abdominal pain from 22 to 96 per cent, of vomiting from 59 to 90 per cent, of

4. (*a*) Robson, A. W. M.: Cancer of the Stomach, London, James Nisbet & Company, Ltd., 1907. (*b*) Friedenwald, J.: A Clinical Study of 1,000 Cases of Cancer of the Stomach, Am. J. M. Sc. **148**:660-670, 1914. (*c*) Stockton, C. C.: Diseases of the Stomach and their Relation to Other Diseases, New York, D. Appleton & Company, 1914. (*d*) Moynihan, B.: Cancer of the Stomach, Practitioner **121**:137-148, 1928. (*e*) Olson, A. E.: Diagnosis and Results in the Treatment of Gastric Cancer, Minnesota Med. **12**:587-589, 1929. (*f*) Nicholson, S. T., Jr.: Consideration of Certain Diagnostic Features of Cancer of the Stomach, Pennsylvania M. J. **34**:169-170, 1930. (*g*) Gray, H. K., and Balfour, D. C.: Cancer of the Stomach, Am. J. Cancer **22**:249-286, 1934. (*h*) Pauchet, V.: La defense de la paroi epigastrique, Bull. et mém. Soc. de chir. de Paris **26**:366-368, 1934. (*i*) Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935. (*j*) Lahey, F. H.; Swinton, N. W., and Peelen, M.: Cancer of the Stomach: Analysis of One Hundred and Ninety-Five Cases with End-Results, New England J. Med. **212**:863-868, 1935. (*k*) Segschneider, W.: Ein Beitrag zur Magenkarzinomstatistik aus der chirurgischen Universitätsklinik zu Bonn, Inaug. Dissert., Bonn, 1935. (*l*) Harris, S.: The Early Symptomatology and the Diagnosis of Gastric Cancer, Am. J. Surg. **31**:225-236, 1936. (*m*) Morlock, C. G., and Hartman, H. R.: The Recognition of Malignant Lesions of the Stomach, in Walters, W.; Gray, H. K., and Priestley, J. T.: Carcinoma and Other Malignant Lesions of the Stomach, Philadelphia, W. B. Saunders Company, 1942, chap. 2. (*n*) Abrahamson, R. H., and Hinton, J. H.: Carcinoma of the Stomach: Review of Four Hundred and Forty-Four Cases to Emphasize the Inadequacy of Present Methods for an Early Diagnosis, Surg., Gynec. & Obst. **71**:135-141, 1940. (*o*) Smithies, F.: Cancer of the Stomach: A Clinical Study of 921 Operatively and Pathologically Demonstrated Cases, Philadelphia, W. B. Saunders Company, 1916. (*p*) MacLean, H.: Modern Views on Digestion and Gastric Diseases, London, Constable & Company, Ltd., 1928, chap. 6. (*q*) Goldie, W.: Analysis of One Hundred and Thirty-Seven Cases of Carcinoma of the Stomach as to Earliest Symptoms, Canad. M. A. J. **20**:486-487, 1929. (*r*) Gatewood, G.: Analytical Survey of Cancer of the Stomach, Ann. Surg. **96**:588-594, 1932. (*s*) Howard, C. P., and Fullerton, C. W.: A Study of Cancer of the Stomach, Canad. M. A. J. **27**:227-236, 1932. (*t*) Oughterson, A. W.: End-Results in the Treatment of Carcinoma of the Stomach, Yale J. Biol. & Med. **4**:711-728, 1932. (*u*) Percy, N. M., and Beilin, D. S.: An Analysis of 1,000 Consecutive Examinations of the Stomach and Duodenum from the Clinical, Roentgenological and Surgical Viewpoints, Am. J. Roentgenol. **32**:179-188, 1934. (*v*) Roof, C. S.: Differential Diagnosis of Gastric Ulcer, Duodenal Ulcer and Cancer of the Stomach as Found in the Study of Three Hundred and Thirty-Seven Hospital Cases, J. Med. **15**:499-512, 1934. (*w*) Chen, K. C.: Clinical Study of One Hundred and Eight Cases of Cancer of the Stomach, Chinese M. J. **52**:177-190, 1937.

constipation from 8 to 80 per cent, of anorexia from 17 to 82 per cent, of general symptoms (including indigestion) from 40 to 69 per cent, of nausea from 20 to 69 per cent and of hematemesis from 7 to 34 per cent. The fact worthy of emphasis here is that few significant differences in the incidence of various symptoms existed between patients with operable gastric cancer and patients with inoperable cancer.

In chart 3 the incidence of the first symptom noted by the patient is given. The same three groupings are used and percentages are listed in the same order: (1) the total number of patients, (2) patients with inoperable gastric cancer and (3) patients with resectable gastric cancer. Pain as a first symptom occurred in 41.0, 39.6 and 46.5 per cent; general symptoms in 18.1, 17.9 and 18.9 per cent; dysphagia in 11.9, 12.8 and 8.3 per cent; anorexia in 8.0, 8.4 and 6.6 per cent; vomiting in

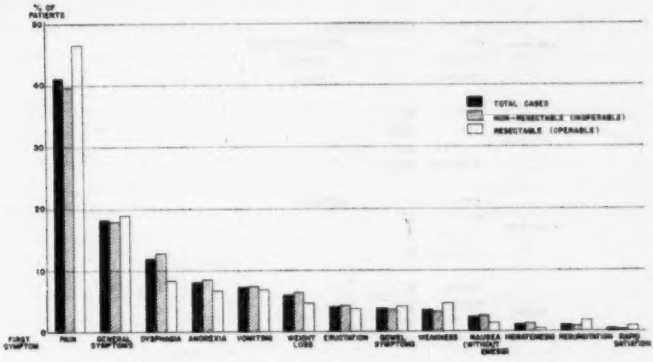

Chart 3.—The incidence of the first symptom noted by 1075 patients (858 inoperable and 217 operable gastric cancers).

7.2, 7.3 and 6.5 per cent; weight loss in 6.0, 6.3 and 4.6 per cent; eructation in 4.1, 4.2 and 3.7 per cent; bowel symptoms in 3.8, 3.7 and 4.1 per cent; weakness in 3.5, 3.3 and 4.6 per cent; nausea in 2.3, 2.6 and 1.4 per cent; hematemesis in 1.1, 1.3 and 0.5 per cent; regurgitation in 1.0, 0.8 and 1.8 per cent, and rapid satiation in 0.4, 0.2 and 0.9 per cent.

The variation in the incidence of the first symptom presented by patients with gastric cancer reported elsewhere is not remarkably different from that reported here and will not be considered in detail.[4] Noteworthy is the similarity of first symptoms among patients with operable gastric cancer and those with inoperable cancer. Of course it would naturally be predictable that the first symptoms registering indel-

ibly on the patients' consciousness would be those not ordinarily experienced, not readily understood and not tolerated with equanimity, such as pain and dysphagia.

In chart 4 bar graphs indicate the relative frequency of weight loss, pain, anorexia, dysphagia, emesis and regurgitation as a first symptom and/or as one of the symptoms presented, according to the location of the cancer in the stomach. The relative frequency of each symptom was not significantly different whether the disease was extensive or

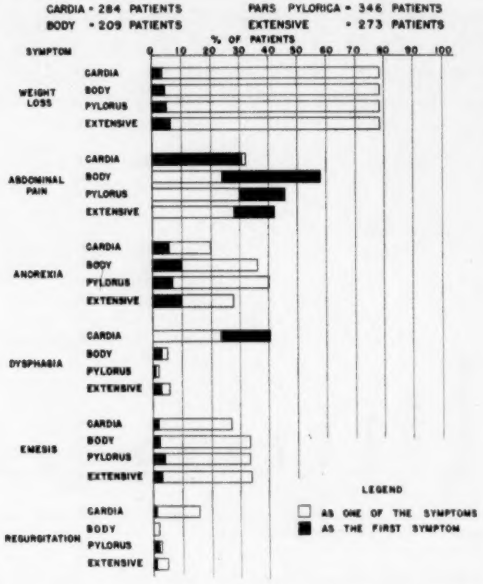

Chart 4.—Bar graphs indicate the frequency of weight loss, pain, anorexia, dysphagia, emesis, regurgitation as a first and/or as one of the symptoms presented, according to the location of the cancer in the stomach. The solid bars indicate the percentage of patients giving the complaint as the first symptom and the open bars the percentage of patients describing the symptom as one of several.

located in the cardia, body or pylorus, except for dysphagia. Dysphagia was the first symptom in 40 per cent of the patients whose cancer was in the cardiac portion of the stomach and occurred with relative infrequency when the involvement was elsewhere in the stomach. The presence of dysphagia in a patient suspected of having cancer of the stomach is highly suggestive of involvement of the cardia. When the cancer was classified as extensive (one half to two thirds of the

stomach involved), it was noted that the symptoms were often milder than when the carcinoma was specifically located, as in the cardia, body or pylorus alone.

The complaint of pain was registered more frequently whenever the body or corpus of the stomach was the site of origin, even more so than in the case of extensive cancer; it has long been a clinical observation that cancers on the lesser curvature (with its greater innervation) evoke pain earlier and in greater degree than involvement of other segments of the stomach. The greater curvature of the fundus is the "silent" region of the stomach and, when the site of cancer, is seldom responsible for pain or for interference with the passage of food. The character of the pain induced by cancers near the cardiac orifice is worthy of comment. This pain is not infrequently referred to the chest, precordium and base of the neck (phrenic?), occasionally radiating down the left arm. An erroneous diagnosis of angina pectoris has sometimes been made, and in fact, some of our patients have been under treatment by cardiologists before the true nature of the disease and its relationship to the pain were discovered.

The greater loss of appetite associated with pyloric and prepyloric cancers is directly an expression of the degree of gastric retention, although this is only relative and there are occasional variations. The more frequent regurgitation caused by cancers of the cardia is readily understandable and is explained by the same mechanism active in producing dysphagia.

DURATION OF SYMPTOMS

Chart 5 shows the duration of symptoms from the known onset to the time of admission to the hospital or clinic in 799 patients whose cancer was inoperable and in 201 patients with resectable gastric cancer. The respective percentages in the 201 patients with resectable cancer and the 799 with inoperable gastric cancer are almost identical, with 4 per cent of each group giving the duration of symptoms as twenty-five to thirty-six months; 8 and 7 per cent as nineteen to twenty-four months; 17 and 23 per cent as ten to eighteen months; 42 and 42 per cent as four to nine months, and 28 and 25 per cent as up to three months. These figures indicate not only that cancer of the stomach may become inoperable before the patient has any symptoms but also that it may be operable even when the symptoms (presumably due to cancer) have been present for two years. We have had numerous instances of patients whose initial symptom or sign heralding the presence of cancer was at the same moment proof of the incurability of the disease (such as a signal node or rectal shelf). Even though the average patient, if untreated, dies within twelve months after the onset of symptoms, there are noteworthy exceptions, such as an instance in which we successfully performed a transthoracic resection of the stomach two

years and three months after the cancer had been pronounced inoperable as the result of exploratory laparotomy and biopsy done in another institution.

In this group of patients the duration of symptoms bore no relation to the resectability of the cancer. Hence no patient should be denied an exploratory operation simply on the basis of having had symptoms or even objective evidence of gastric cancer for many months, nor should any physician extend too much hope to a patient's family simply because the cancer has been discovered "early" so far as the duration of symptoms is concerned.

Other reported statistics [5] show that from 35 to 75 per cent of patients had symptoms for six months or less, 10 to 35 per cent for six

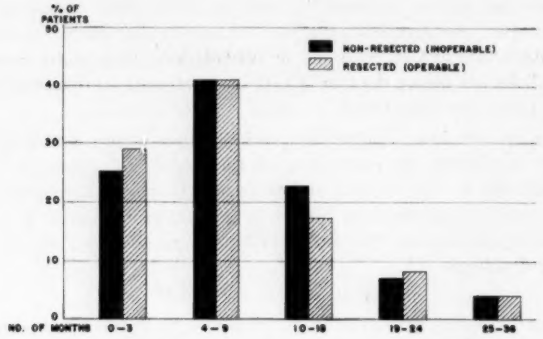

Chart 5.—The duration of symptoms from known onset to time of admission to the hospital or clinic in 799 patients whose cancer was inoperable and in 201 patients with resectable gastric cancer.

5. Osler, W., and McCrae, T.: Cancer of the Stomach; Clinical Study, Philadelphia, P. Blakiston's Son & Company, 1900. Fenwick, S., and Fenwick, W. S.: Cancer and Other Tumours of the Stomach, London, J. & A. Churchill Company, 1902. Cabot, H., and Adie, G. C.: Etiology of Cancer of the Stomach: A Review of One Hundred and Sixteen Cases of Cancer of the Stomach with Particular Relation to Etiology, Ann. Surg. **82**:88-108, 1925. Lloyd, N. L.: Cancer of the Stomach, an Analysis of Fifty Cases at Guy's Hospital, Guy's Hosp. Rep. **75**:410-427, 1925. Crohn, B. B.: Affections of the Stomach, Philadelphia, W. B. Saunders Company, 1927. McVicar, C. S., and Daly, J.: Diagnosis of Operable Carcinoma of the Stomach, Ann. Int. Med. **1**:145-160, 1927. Knüpper, H.: Fünf Jahre Chirurgie des chronischen Geschwürs und Karzinoms des Magens der chirurgischen Universitätsklinik zu Leipzig, Inaugur. Dissert., Leipzig, 1930. Saltzstein, H. C., and Sandweiss, D. S.: The Problem of Cancer of the Stomach, Arch. Surg. **21**:113-127 (July) 1930. Boas, I.: Early and Tentative Diagnosis of Cancer of the Gastro-Intestinal Tract, Am. J. Cancer **15**:1586-1589, 1931. Delort, M., and Blanc-Champagnac, J.: Le valeur diagnostique du "debut recent" dans le

to twelve months, 11 to 25 per cent for one to two years and 7.5 to 14.8 per cent for two to five years. Lahey and Jordan [6] failed to find any correlation between the duration of symptoms and the resectability of gastric cancer.

Saypol and Hinton [7] gave a similar distribution for the duration of symptoms and pointed out that among their 196 patients there was a higher incidence of resectable gastric cancer in the group having symptoms for six months to three years than in the group having symptoms for one to six months. Lawrence and Kay [8] reported that 41 per cent of their 201 patients with gastric cancer had symptoms for less than six months, 20.8 per cent for six to twelve months, 25 per cent for one to two years, 2.5 per cent for two to three years and 10 per cent for more than three years or for an unknown time. Thirty-eight per cent

cancer de l'estomac, Bull. et mém. Soc. de med. de Paris. **17**:645, 1931. Hernando, T.: Como empieza el cancer del estomago (los antecedentes. los primeros sintomas), Prog. clin. **39**:785-804, 1931. Newcomb, W. D.: Relationship Between Peptic Ulcer and Gastric Carcinoma, Brit. J. Surg. **20**:279-308, 1932. Else, J. E., and Schneider, O.: Cancer of the Stomach, Northwest Med. **32**:323-326, 1933. Streicher, M. H., and Kuehl, M. L.: Comparative Analysis of Gastric Cases Observed for Period April 1925 to April 1932, Illinois M. J. **63**:340-343, 1933. Whipple, A., and Raiford, T. S.: The Type and Grade of Cancer of the Stomach in Relation to Operability and Prognosis, Surg., Gynec. & Obst. **59**:397-409, 1934. Landon, L. H.: The Gastric Ulcer-Cancer Problem, Ann. Surg. **101**:536-549, 1935. Horsley, J. S.: Incidence, Diagnosis and Treatment of Cancer of the Stomach, M. Ann. District of Columbia **4**:185-190, 1935. Howze, H. H.: Differential Diagnosis of Gastric and Duodenal Ulcer and Carcinoma of the Stomach, Med. Bull. Vet. Admin. **12**:62-66, 1935. Hunt, J. C.: Diagnosis and Management of Cancer of the Stomach, J. Missouri M. A. **32**:431-434, 1935. Raven, R. W.: Prognosis of Cancer of the Stomach, St. Barth. Hosp. Rep. **68**:263-270, 1935. Snell, A. M., and Kirklin, B. R.: Diagnosis of Gastric Carcinoma, Journal-Lancet **55**:153-157, 1935. Carvaillo: Diagnostic precose des neoplasmes de l'estomac et de l'intestin, J. de med. de Paris **56**:492-494, 1936. Maes, U., and McFetridge, E. M.: The Place of Surgery in the Therapy of Peptic Ulcer, New York State J. Med. **36**:1399-1404, 1936. Minnes, J. F., and Geschickter, C. F.: Clinical Features of Gastric Cancer, Am. J. Cancer. **27**:740-748, 1936. Comfort, M. W., and Butsch, W. L.: Differential Diagnosis of Benign and Malignant Small Lesions of the Stomach: An Attempt to Evaluate Statistically the Various Symptoms and Laboratory Findings, Am. J. Surg. **35**:515-523, 1937. Snowden, R. R.: The Importance of Definitely Establishing the Diagnosis in Every Case of Suspected Carcinoma of the Stomach, Internat. Clin. **2**:116-130, 1937. Kiefer, E. D.: Carcinoma of the Cardiac End of the Stomach, Surg. Clin. North America **18**:661-670, 1938. Levitt, A., and Argue, J. F.: Clinical and Pathological Manifestations of Cancer of the Stomach, Am. J. Digest. Dis. **4**:818-820, 1938. Footnote 4*o* to *w*.

6. Lahey, F. H., and Jordan, S. M.: Cancer of the Stomach, New England J. Med. **210**:59-66, 1934.

7. Saypol, G. M., and Hinton, J. H.: Statistical Review of Carcinoma of the Stomach, Am. J. Surg. **54**:431-434, 1941.

8. Lawrence, E. A., and Kay, J. H.: Carcinoma of the Stomach: A Ten Year Survey Made in a General Hospital, Surgery **19**:504-514, 1946.

of these patients whose gastric cancer was inoperable had symptoms for less than three months as compared to 27 per cent who underwent gastrectomy. Twenty-two per cent of the patients with operable gastric cancer had symptoms for nine months to a year as compared with 12 per cent whose cancer was considered inoperable.

The impression of most investigators up to the present seems to be that, in general, cancer associated with a somewhat longer history tends to be resectable more often than that associated with a short history. No one, however, can say how long a tumor may have been present before it caused symptoms. These findings should in no way dull the zeal with which gastrointestinal complaints are investigated since it is impossible to overemphasize the fact that a small early cancer is easier to remove and less likely to have metastasized than one of greater extent and longer duration.

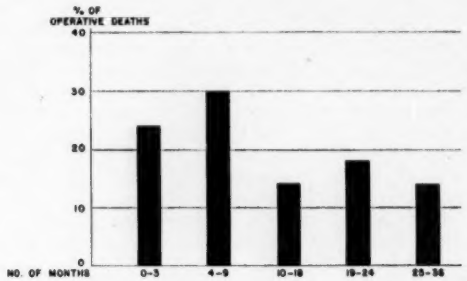

Chart 6.—The percentage of operative deaths according to the duration of symptoms in 45 patients who died after gastrectomy.

In chart 6 the percentage of operative deaths is presented according to the duration of symptoms. From charts 5 and 6 it is evident that the surgical mortality is three times as great among patients whose symptoms had been present from nineteen to thirty-six months, since 14 of the 20 patients (70 per cent) in this category failed to survive operation. Although the number of patients is small, these differences suggest the importance of the state of nutrition as a guide in evaluating the operative risk. Perhaps the administration of plasma or protein hydrolysates and careful preoperative management may now make such patients better surgical risks.

Ten years ago Pack and Gallo [9] analyzed a large number of case records of cancer in an attempt to determine the responsibility for the delay in treatment. A delay of three months or more from the time of

9. Pack, G. T., and Gallo, J. S.: The Culpability for Delay in the Treatment of Cancer, Am. J. Cancer **33**:443-462, 1938.

discovery of symptoms to the visit to the physician was regarded as undue delay on the part of the patient. Criticism of the physician was based on the action taken by the first physician. The patient alone was responsible for 44.3 per cent of the delays, the patient and the physician for 18.0 per cent and the physician alone for 17.0 per cent; in 20.7 per cent there had been no delay. A similar study recently completed by Leach and Robbins [10] using the same source material showed improvement in the alertness of the patient but the same or uncorrected culpability of the physician.

CHANGE OF SYMPTOMS

There were 155 patients who had gastrointestinal symptoms for more than two years; of these 53 presented a history of ulcer-like symptoms and 102 gave a vague story of indigestion. By "ulcer-like" we mean that these patients had abdominal pain, usually coming on when the stomach was empty and relieved by the intake of food or sodium bicarbonate. Those with "indigestion" complained of vague abdominal pain, epigastric fulness, gas, belching, heartburn and the like, usually coming on after eating and most frequently being relieved by belching. These two groups are further divided into patients whose gastric cancer was resectable and patients whose cancer could not be removed surgically.

Chart 7 shows the time of change in the symptoms presented by the four groups of patients before the diagnosis of cancer had been established. In all but 2 of the patients with a history of ulcer-like symptoms there was a warning manifested by a change in symptoms. This was usually marked by increasing pain, no longer so effectively relieved by diet and medication and accompanied with anorexia and loss of weight. On the basis of symptomatology alone, it would seem to the clinician that the change in symptoms might indicate the development of cancer of the stomach succeeding an ulcer, but the gross and microscopic examination of the resected specimens almost never furnishes evidence of preexisting benign ulcer. The true clinical significance, therefore, of this change of symptoms is not the academic point of the so-called carcinomatous degeneration of a gastric ulcer, but practically it constitutes a warning that the ulcer is probably neoplastic and requires surgical treatment.

The time of change in the type of symptoms was not found to be significantly different in patients whose gastric cancer was resected and those in whom it was considered inoperable. However, in all but 4 of the patients with a history of ulcer-like symptoms a change of

10. Leach, J. E., and Robbins, G. F.: Delay in Diagnosis of Cancer, J. A. M. A. **135**:5-8 (Sept. 6) 1947.

symptoms was noted one to six months before discovery of the cancer in 60 per cent and seven to twelve months before diagnosis of the cancer in approximately 20 per cent. The remainder of these patients noted a change in symptoms thirteen or more months before their disease was correctly diagnosed.

The group of patients with a history of indigestion presented similar findings except that 20 per cent of them experienced no change in symptoms. In 58 per cent increasing distress developed over a period of from one to six months prior to the recognition of their gastric cancer. Twenty-two per cent of patients whose gastric cancer was considered inoperable noted a change of symptoms seven to twelve months before the diagnosis of cancer was made. Four per cent of the group with inoperable cancer had experienced increasing or different symptoms for thirteen or more months prior to the diagnosis of cancer. Again the time of change in the type of symptoms is not significantly

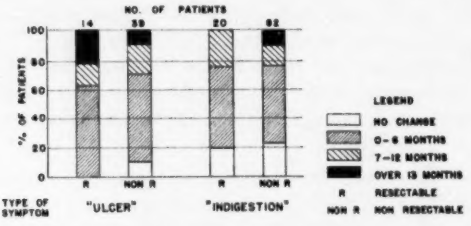

Chart 7.—The time of change in symptoms presented by 155 patients who had gastrointestinal symptoms for more than two years is shown. Of these, 53 (14 with resectable and 39 with inoperable cancer) gave a history of ulcer-like symptoms and 102 (20 with resectable and 82 with inoperable cancer) gave a vague history of indigestion. The open bars indicate the percentage of patients who experienced no change in symptoms up to six months before definitive diagnosis, the coarse cross-hatched bars the percentage who had symptoms seven to twelve months before a diagnosis of cancer of the stomach was established and the solid bars the percentage who had symptoms thirteen months or longer before the diagnosis was established. Discussion of this chart is in the text.

different for the patients with operable gastric cancer and those with inoperable cancer.

Whether this change in symptoms in patients with a history of indigestion represents simple progression of the carcinoma or development of gastric cancer in a patient with functional gastrointestinal symptoms cannot be considered here. However, it is obvious that patients who continue to complain of vague but persistent abdominal distress deserve most careful scrutiny despite previous negative findings. Gastrointestinal symptoms should be subjected to qualitative reanalysis on each visit despite "normal" findings three, six, nine or twelve months previously.

It has often been suggested that physicians are justified in insisting that a series of gastrointestinal roentgenograms be a routine part of the yearly health examination in all patients over 40 years of age. About twelve years ago at the Memorial Hospital one hundred consecutive roentgenographic studies were made on patients of this age who had no gastric complaints, and in this group one early cancer of the stomach was discovered and resected; the patient is now living and well more than a decade after surgical treatment. More recently, the Strang Clinic of the Memorial Hospital[11] has been pursuing this elective gastrointestinal study diligently; of 1,600 patients without gastric symptoms who have been investigated to date, 3 were found to have malignant tumors, namely, a myosarcoma of the esophagus and two early and resectable cancers of the stomach.

Swenson,[12] who has had much experience with the so-called "mass" roentgenologic study of the stomachs of apparently well persons, offers this realistic yet humorous thought concerning the practicality of such procedures as routine in the attempted early detection of gastric cancer. To maintain a roentgenologic surveillance of the 42,000,000 Americans over 40 years of age would require the constant services of 1,809 radiologists working forty-eight weeks of every year and examining 1 new patient every four minutes. He adds, parenthetically, that the total number of diplomates in radiology is only 2,300.

PHYSICAL FINDINGS

In chart 8 the pertinent physical findings in 1,110 patients with gastric cancer are summarized in the order of their frequency. A definitely palpable mass was present in 494, or 45.4 per cent; cachexia and/or emaciation in 216, or 19.4 per cent; abdominal tenderness in 188, or 16.9 per cent; a questionable mass in 114, or 10.3 per cent; metastasis to palpable superficial lymph nodes in 60, or 5.4 per cent; metastasis to other organs such as the liver, pelvic viscera or perirectal tissues in 34, or 3 per cent; ascites in 25, or 2.2 per cent; abdominal distention in 18, or 1.6 per cent; increased peristalsis in 11, or 1 per cent; spasm of abdominal muscles in 4, or 0.3 per cent, and jaundice in 4, or 0.3 per cent.

In a consecutive series of 149 patients whose gastric cancers were resected, 20, or 13 per cent, had large palpable livers not caused by metastasis. A palpable liver, therefore, is only significant because of its nodularity and firmness; aspiration biopsy of the liver through the intact abdominal wall has often been successful in our hands as a means of obtaining a positive diagnosis of carcinoma.

11. Strang Clinic, Memorial Hospital, New York. Personal communication to the authors.

12. Swenson, P. C.: Mass Survey of the Gastro-Intestinal Tract, South. M. J. **41**:108-112 (Feb.) 1948.

In the majority of instances when we suspect hepatic metastasis or peritoneal carcinosis secondary to gastric cancer and cannot prove it by physical examination alone, we resort to peritoneoscopy under local anesthesia. In a series of cases in which this suspicion existed the peritoneoscope in our hands verified the presence of metastasis in 50 per cent of the patients. The great value of this diagnostic aid is apparent when it is realized that 50 per cent of these patients were spared the discomforts, hazards, uselessness and expense of an exploratory laparotomy.[13]

Although a palpable mass is more frequently associated with inoperable gastric cancer, its presence certainly does not indicate a hopeless prognosis. In fact, the bulky, polypoid, intragastric tumors are often more easily resected than the nonpalpable infiltrating type. The size

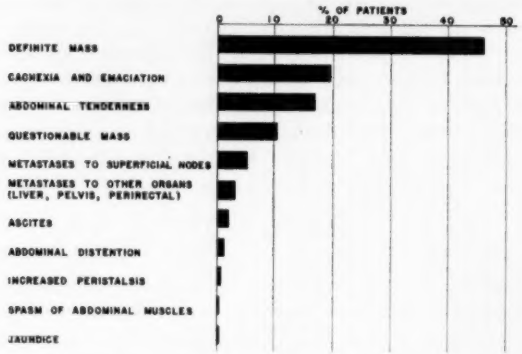

Chart 8.—The pertinent physical findings in 1,110 patients with gastric cancer in the order of their frequency.

of the gastric cancer and even its apparent fixity as determined on abdominal palpation should not contraindicate surgical intervention.

In table 1 the incidence of the presence or absence of an abdominal mass is compared in 191 patients who underwent gastric resection and in 723 patients whose cancer was considered inoperable. A tumor was palpable in 41.8 per cent of the former and in 57.4 per cent of the latter; an indefinite mass or sense of epigastric resistance was described in 13.6 and 12.2 per cent, respectively. Although the tumor was palpable in a relatively high percentage of patients, abdominal tenderness was recorded in only 17 per cent of the total number of patients.

13. Narancio, M. M.; Pierson, J. C.; McNeer, G., and Pack, G. T.: The Economic Value of Peritoneoscopy, Ann. Surg. **121**:185-190, 1945.

Of the 216 patients (19.4 per cent) with cachexia and/or emaciation, 80, or 13.9 per cent, had gastric cancers in a stage permitting resection, which confirms our long-held opinion that these symptoms do not constitute sufficient reasons for classifying a particular case as one of inoperable gastric cancer. Yet the sad fact exists that recorded observations at necropsy from numerous sources dating from the time of Billroth up to 1940 reveal that patients dying with gastric cancer have the disease confined to the stomach and perigastric lymph nodes in 20 to 25 per cent of the cases.[2]

Of the 60 patients with demonstrable metastasis to accessible superficial (palpable) lymph nodes, 38 had involvement of the so-called sentinel or signal node of Troisier and Virchow in the neck and 9 had metastasis in inguinal or femoral lymph nodes, 7 in axillary nodes, 3 in the umbilicus, 2 in intercalated nodes in the abdominal wall and 1 in multiple regional nodes.

TABLE 1.—*Significance of the Presence or Absence of an Abdominal Mass in 914 Patients with Carcinoma of the Stomach*

Findings	Percentage of Cases	
	191 Cases of Operable Cancer	723 Cases of Inoperable Cancer
Definite mass	41.8	57.4
Indefinite mass	13.6	12.2
No mass	44.5	30.5

In a study of the significance of the supraclavicular signal node in patients with abdominal and thoracic cancer, Viacava and Pack[14] in 1944 reviewed the data on 883 patients with cancer of the stomach. Twenty-three of these (2.6 per cent) had metastatic involvement of the Troisier-Virchow node, and in 17 the recognition of the abnormal node was the first recognizable evidence of the cancer. In 15 patients the left node was involved, in 3 patients the right node, and in 5 patients the metastasis occurred bilaterally to the neck.

Obvious metastasis to the liver was recognized in 11 patients; metastasis to the perirectal tissue (the rectal shelf of Blumer) could be palpated in 18 patients, and other pelvic organs were found implicated on physical examination of 5 patients. The 25 patients with ascites and the 4 with jaundice were immediately considered as having inoperable gastric cancers. An analysis of these physical findings reveals that on this basis alone 11 per cent of the patients examined had one or more

14. Viacava, E. P., and Pack, G. T.: Significance of Supraclavicular Signal Node in Patients with Abdominal and Thoracic Cancer: A Study of One Hundred and Twenty-Two Cases, Arch. Surg. **48**:109-119 (Feb.) 1944.

signs indicating the inoperability of the gastric cancer. In the study of these 1,000 case histories, one encounters now and then the tragic fact that the first presenting sign or symptom experienced by the patient is indicative of the incurability of the gastric cancer—a signal node in the neck, an enlarging abdomen due to ascites without antecedent indigestion, diffuse lymphatic pulmonary carcinosis from a silent cancer of the stomach or rectal obstruction caused by metastasis from an unrecognized primary source.

LABORATORY DIAGNOSTIC STUDIES IN CASES OF GASTRIC CANCER

Achlorhydria occurs in from 40 to 60 per cent of patients with gastric cancer and is a useful, although often misleading, factor in establishment of the diagnosis. This is particularly true in patients 55 years of age or older with achlorhydria, since 15 to 20 per cent of normal persons in this age group may fail to secrete hydrochloric acid with or without histamine stimulus.[15] Perhaps even more confusing is the patient in this age group who has a gastric ulcer with a low amount of free hydrochloric acid but who must be considered to have gastric carcinoma until this is disproved. Despite such limitations, gastric analysis is done routinely in investigating gastric complaints and serves to strengthen the physician's suspicions of the possibility of cancer when achlorhydria is present. The presence of free hydrochloric acid is of no significance in ruling out carcinoma of the stomach. At best, gastric analysis can be considered only one of a series of tests which may or may not be of confirmatory significance but which should never be allowed to give the physician a false sense of security or to influence too much the decision whether to explore the abdomen or to handle the patient's symptoms medically. The results of gastric analyses in 493 patients with carcinoma of the stomach seen at the Memorial Hospital are summarized in tables 2 and 3 and bear out these statements.

All the patients were given histamine, and analyses of the gastric contents for free and total hydrochloric acid were done on fasting samples and on samples aspirated at thirty minutes, one hour and two hours after the subcutaneous injection of 0.5 mg. The patients were also classified according to the location of the cancer in the stomach, i. e., cardia, body, pylorus or extensive (table 2). Achlorhydria was present in 63.7 per cent of 493 patients; the amount of acidity varied from 1 degree to 40 degrees in 17.3 per cent, was within normal limits (40 to 65 degrees) in 9.5 per cent and was excessive in 9.5 per cent. When these figures are broken down according to the location of the

15. Comfort, M. W., and Butsch, W. L.: Gastric Acidity in Cases of Benign and Malignant Lesions of the Stomach, Proc. Staff Meet. Mayo Clin. **11**:440-446, 1936.

cancer, the percentages are approximately the same and the differences are not statistically significant except for the 10 per cent increase in achlorhydria whenever the cancer was described as extensive.

In table 3 the incidence of achlorhydria in 358 patients with inoperable cancers of the stomach and in 135 patients who underwent gastric resection is presented according to the location of the neoplasm. When the cancer involved the pylorus, acidity was present in 62.2 per cent of patients with inoperable disease and in 42.7 per cent of patients whose cancers were resected. The percentages for the body were 67.9

TABLE 2.—*Gastric Analysis in Carcinoma of the Stomach*

Location of Tumor	Number of Cases	Percentage of Cases			
		Achlorhydria	Low Hydrochloric Acid Content (1 to 40)	Normal Hydrochloric Acid Content (40 to 65)	High Hydrochloric Acid Content
Total	498	63.7	17.3	9.5	9.5
Pylorus	169	55.6	20.7	11.8	11.8
Body	106	65.0	17.0	7.6	10.4
Cardia	91	63.8	17.6	9.9	8.8
Extensive	127	73.3	12.6	7.9	6.3

TABLE 3.—*Incidence of Achlorhydria in 493 Patients with Operable and Inoperable Gastric Cancer*

Location of Tumor	Total Cases		Patients with Operable Cancer		Patients with Inoperable Cancer	
	No.	Percentage with Achlorhydria	No.	Percentage with Achlorhydria	No.	Percentage with Achlorhydria
Total	493	63.7	135	51.1	358	65.0
Pylorus	169	55.6	82	42.7	87	62.2
Body	106	65.0	24	54.8	82	67.9
Cardia	91	63.8	8	25.0	83	69.8
Extensive	127	73.3	21	90.5	106	69.9

and 54.8 per cent, respectively, and for the cardia 69.8 and 25 per cent; when the involvement was extensive anacidity was present in 69.9 and 90.5 per cent. In general, achlorhydria was essentially the same no matter where the site when the cancer was inoperable. When the cancer was resectable, there was a 20 per cent decrease in the incidence of anacidity when the disease involved the pylorus, a 13 per cent decrease when the body of the stomach was involved and a 44 per cent decrease when the cardia was the site of the tumor. Paradoxically, when the involvement was described as extensive, a 20 per cent increase in achlorhydria was noted among the patients with resectable cancer. For the entire group, the incidence of achlorhydria was 14.0 per cent less when the patient had resectable gastric carcinoma than when the cancer

was inoperable. The incidence of achlorhydria in cases of extensive gastric carcinoma is 10 per cent greater than when the disease is confined to one portion of the stomach for the group as a whole and twice as great among patients with operable cancer.

In table 4 anacidity and the variation in degree of acidity are presented according to the histologic grading and the size of the tumor in 142 patients in whom gastric resection was performed. No striking differences were noted in the incidence of achlorhydria or degree of acidity according to the histologic grading of the cancer. It is of interest that although the number of patients is small excessive acidity was more frequent in cases of ungraded and grade 4 carcinoma. The incidence

TABLE 4.—*Studies in Gastric Acidity on Patients with Resectable Gastric Carcinoma*

		Percentage of Cases					
				Degree of Acidity			
Group	Total Cases	Achlorhydria	Free Hydrochloric Acid Present	1 to 20	20 to 40	40 to 60	Over 60
Histologic Grading:							
Total cases	142	50.0	50.0	8.4	16.2	3.5	21.9
Ungraded	5	60.0	40.0	0.0	0.0	0.0	40.0
Grade I	12	41.7	58.3	0.0	8.3	0.0	50.0
Grade II	44	47.7	52.3	6.8	22.7	2.3	20.5
Grade III	54	46.3	53.7	14.8	16.7	5.6	16.6
Grade IV	27	63.0	37.0	3.7	11.1	3.7	18.5
Size of Tumor:							
1 to 4 cm.	10	10.0	90.0	10.0	20.0	10.0	50.0
4 to 6 cm.	19	52.6	47.4	21.1	5.25	5.25	15.8
6 to 9 cm.	28	53.6	46.4	7.1	17.8	3.6	17.9
9 to 12 cm.	12	75.0	25.0	0.0	8.3	0.0	16.7

of anacidity apparently increases directly in proportion to the size of the tumor; it was present in 1 of 10 patients with a cancer 4 cm. or less in size, whereas 9 of 12 patients with tumors 9 cm. or larger had anacidity. Among 47 patients with carcinomas 4 to 9 cm. in size, 25 exhibited achlorhydria.

In table 5 a comparison of the incidence of anacidity as well as the distribution according to the degree of acidity in 75 normal adults 60 to 64 years of age,[16] 81 patients with benign gastric ulcer at the Memorial Hospital and 135 patients who had resectable gastric cancer is made. Anacidity was present in 23.0 per cent, 7.4 per cent and 51.1 per cent respectively. For the three groups 7.3, 7.4 and 8.2 per cent of the total number had 1 to 20 degrees of free hydrochloric acid after histamine was given; 28.0, 14.9 and 14.8 per cent 20 to 40 degrees; 27.1, 14.9

16. Vanzant, F. R.; Alvarez, W. C.; Eusterman, G. B.; Dunn, H. L., and Berkson, J.: The Normal Range of Gastric Acidity from Youth to Old Age; An Analysis of 3,749 Records, Arch. Int. Med. **49**:345-359 (March) 1932.

and 4.4 per cent 40 to 60 degrees, and 14.6, 54.4 and 21.4 per cent more than 60 degrees of free hydrochloric acid. Thus 135 patients with gastric cancer showed anacidity twice as frequently as normal persons and nearly seven times as often as patients with benign gastric ulcers. Free hydrochloric acid was present in amounts above 60 degrees in the group with ulcer twice as frequently as in patients with carcinoma and more than three times as often in normal adults of 60 to 64 years of age. Low acidity (1 to 20 degrees) was almost identical for the three types; 20 to 40 degrees of acidity was twice as frequent among normal persons as among patients with benign ulcer or with cancer; normal acidity (40 to 60 degrees) was encountered twice as frequently among normal

TABLE 5.—*Studies of Gastric Acidity Comparing Normal Adults and Patients with Benign Gastric Ulcer and Resectable Gastric Carcinoma*

		Percentage of Cases					
				Degree of Acidity			
Group	Total Cases	Achlorhydria	Free Hydrochloric Acid Present	1 to 20	20 to 40	40 to 60	Over 60
Normal persons* (men, age 60 to 64)	75	23.0	77.0	7.3	28.0	27.1	14.6
Benign gastric ulcers	81	7.4	92.6	7.4	14.9	14.9	54.4
Gastric carcinoma	135	51.1	48.9	8.2	14.8	4.4	21.4
Location of tumor:							
Pylorus	82	42.7	57.3	6.1	17.1	6.1	28.0
Body	24	54.3	45.7	16.7	16.7	0.0	12.5
Cardia	8	25.0	75.0	25.0	12.5	0.0	37.5
Extensive	21	90.5	9.5	0.0	4.7	4.7	0.0

* Vanzant, F. R.; Alvarez, W. C.; Eusterman, G. B.; Dunn, H. L., and Berkson, J.: The Normal Range of Gastric Acidity from Youth to Old Age; An Analysis of 3,746 Records, Arch. Int. Med. 49: 345-359 (March) 1932.

persons as among patients with gastric ulcer and seven times more often than in patients with gastric carcinoma.

If the data on degree of acidity are computed from the number of patients who had free hydrochloric acid rather than from the percentage of the total number of patients in each group, somewhat different results are obtained. In the 1 to 20 degree classification are found 18.4 per cent of the normal persons, 7.4 per cent of those with ulcers and 16.9 per cent of those with cancer; in the 20 to 40 degree classification 36.8, 14.9 and 32.4 per cent; in the 40 to 60 degree classification 35.5, 14.9 and 6.0 per cent, and in the above 60 degree classification 9.3, 54.4 and 43.6 per cent respectively. The spread in the degree of anacidity is not nearly so great when the data are considered in this way, which suggests that when free hydrochloric acid is present in a patient with gastric cancer the degree of acidity gives no clue to the presence or absence of the cancer.

In table 6 the results of the gastric analysis are presented according to the gross description of the tumor: ulcerating, infiltrating, annular, polypoid and the combinations encountered in the gross pathologic descriptions of 134 tumors. Perhaps of interest is the relatively high incidence of anacidity in cases of polypoid (83.5 per cent) and infiltrating (72.6 per cent) tumors, although when all combinations are considered the incidence of achlorhydria falls to 54 and 61 per cent, respectively, for the two groups. It has been stated by one group of investigators [17] that all polypoid growths studied by them were associated with achlorhydria.

TABLE 6.—*Gastric Analysis in Relation to Macroscopic Type of Operable Gastric Cancer*

		Gastric Analysis							
		Achlorhydria		Free Hydrochloric Acid Present		Degree of Acidity			
Macroscopic Type	Total Cases	No.	%	No.	%	1 to 20	20 to 40	40 to 60	Over 60
Total cases	134	69	51.4	65	48.6	12	19	4	30
Ulcerating	46	17	37.0	29	63.0	6	5	1	17
Ulcerating and infiltrating	21	15	71.3	6	29.7	3	2	..	1
Ulcerating and polypoid	10	6	60.0	4	40.0	..	1	1	2
Ulcerating and annular	8	3	37.5	5	62.5	..	4	..	1
Ulcerating, infiltrating and annular	5	2	40.0	3	60.0	..	1	..	2
Ulcerating, infiltrating and polypoid	2	1	50.0	1	50.0	1	..	..	..
Ulcerating, infiltrating, polypoid and annular	2	1	50.0	1	50.0	..	1	..	..
Polypoid	12	10	83.5	2	16.5	..	1	..	1
Polypoid and infiltrating	3	1	33.3	2	66.7	..	1	1	..
Polypoid and annular	1	..	....	1	100.0	..	1	..	..
Infiltrating	11	8	72.6	3	27.4	1	..	..	2
Infiltrating, polypoid and annular	3	1	33.3	2	66.7	..	..	1	1
Annular	7	3	23.3	4	76.7	..	1	..	3
Annular and infiltrating	2	1	50.0	1	50.0	1	..	..	..
In situ	1	..	....	1	100.0	..	1	..	..

Hydrochloric acid is produced by the parietal cells of the gastric mucosa which are contained primarily in the cardia and body of the stomach. The observation that achlorhydria in cases of gastric cancer is not related to the site of the neoplastic process suggests that destruction of acid-forming cells of the mucosa is not the only cause of the absence of free hydrochloric acid in the gastric juices of patients with carcinoma of the stomach. The decision as to whether this observation can be explained by the assumption that the presence of carcinoma per se inhibits the excretion of hydrochloric acid or enterogastrone or that there is an excessive formation of mucus or inflammatory exudate (acid-binding protein) in the gastric juice of such patients awaits further investigation.

17. Wangensteen, O. H.: The Problem of Gastric Cancer, J. A. M. A. **134**:1161-1169 (Aug. 2) 1947.

From these data it would appear that the presence of achlorhydria or low acidity in a patient suspected of having cancer of the stomach is a useful confirmatory finding but is by no means diagnostic of the disease. The history, physical findings and other laboratory data, including roentgen studies and gastroscopy reports, must all be available before the disease can be ruled out or an early diagnosis established. The data on all patients for whom gastric analysis was made revealed that anacidity did not influence operability or operative mortality.

Analyses for lactic acid or search for the Boas-Oppler bacillus in the gastric contents was carried out too infrequently in these patients to justify reporting the results, although the presence of either or both in the gastric contents is almost always an indication of retention of the gastric contents, usually due to pyloric obstruction. However, such findings give no indication of the benign or malignant character of the disease causing the obstruction.

Gross blood was noted in the gastric contents in 36.6 per cent of the analyses done. The significance of this observation is, of course, always clouded by the possibility that the blood may have resulted from mechanical trauma during passage of the tube. Should the aspirated material be grossly bloody or coffee ground in character, the assumption that a bleeding lesion is present in the esophagus or stomach is justifiable, and such lesions are more frequent in patients with gastric cancer than in those with gastric or duodenal ulcer.

Recently the gastric contents have been centrifuged and the residue examined for the presence of cancer cells by the method of Papanicolaou. Incomplete studies [18] indicate that, although this is one of the most difficult methods of cytologic study, it promises to be highly rewarding in establishing the preoperative diagnosis of cancer. With further experience and expert training, this technic will undoubtedly have wide application. Perhaps further study of the chemical and biologic constituents of gastric juice, including the acids, salts, protein and enzyme content or other secretory functions, may give additional data useful for establishing the diagnosis of gastric cancer.

Determination of the presence or absence of occult blood in the stool was not done in enough patients to justify reporting the data. However, it has long been known and taught that the persistent presence of occult blood in the stool of a patient on a meat-free diet, when there is no obvious source such as hemorrhoids, ulcerative lesions of the colon or intestinal purpura, is highly suggestive of carcinoma of the stomach or small intestines. A limitation on the usefulness of this

18. Papanicolaou, G.: Personal communication to the author.

finding is the fact that not all gastric carcinomas bleed; hence the absence of occult blood in the stool should never give the physician a sense of security.

THE ANEMIA OF PATIENTS WITH GASTRIC CARCINOMA

The incidence and degree of anemia in 844 patients with gastric cancer is indicated in table 7, with patients grouped according to the location of the disease in the stomach and separated into those whose cancer was resectable and those in whom it was considered inoperable. In general, no significant differences in the incidence and degree of anemia according to the segmental location of the cancer or its operability are apparent. In chart 9 these same data are presented in bar graphs indicating the percentage of the total number of patients, the patients with inoperable cancer and the patients whose gastric cancer

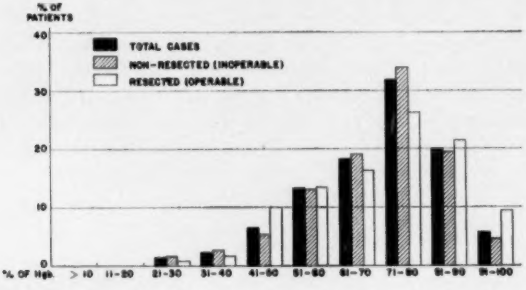

Chart 9.—The percentage of patients with varying degrees of anemia is shown. Initial hemoglobin content of 844 patients (631 with inoperable and 213 with operable gastric cancers). The solid, cross-hatched and open bars indicate the percentage of the total number of patients, patients with inoperable gastric cancer and patients with cancers considered operable.

was resected, with hemoglobin contents varying, in increments of ten, from 21 to 100 per cent. This emphasizes the statement made that the degree of anemia gives no clue to the operability of gastric cancer.

Oppenheim, Abels, Pack and Rhoads[19] studied the type of anemia observed in 122 patients in this series. Seventy-eight patients (64 per cent) had abnormally low red blood cell counts and concentrations of hemoglobin. No correlation was found between the existence of achlorhydria and the incidence or severity of the anemia. Of the 78 patients, the mean erythrocyte volume was macrocytic in 25, normocytic in 35

19. Oppenheim, A.; Abels, J. C.; Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Cancer of the Gastro-Intestinal Tract: XIX. The Anemia of Patients with Gastric Carcinoma, J. A. M. A. **127**:273-276 (Feb. 3) 1945.

and microcytic in 18. In the patients with macrocytosis, hyperchromia, normochromia and hypochromia were found in 1, 24 and none, respectively. The usual type of anemia associated with gastric cancer is normochromic.

The microcytosis of patients with gastric cancer cannot be entirely explained by the usual causes, namely, dietary deficiency of iron or a great loss of iron through chronic bleeding, although 10 of the 18 patients gave a history of, or were found in the hospital to have, a significant quantity of gastrointestinal bleeding. Three grains of ferrous sulfate was administered orally to 3 of the patients with microcytic hemograms for thirty-eight to forty days, with an increase in red blood cell counts only from 100,000 to 250,000 and in concentration of hemoglobin from 8 to 13 per cent.

TABLE 7.—*Hemoglobin Content in Relation to Location of Gastric Cancer*

Location	Total Cases	Percentage of Cases: Under 31%	31 to 40%	41 to 50%	51 to 60%	61 to 70%	71 to 80%	81 to 90%	91 to 100%
Grand Total	844	1.4	2.4	6.6	13.3	18.5	32.0	20.0	5.8
Operable	213	0.9	1.4	10.0	13.6	16.4	26.2	21.6	9.4
Inoperable	631	1.6	2.7	5.4	13.2	19.2	34.0	19.5	4.6
Pylorus:									
Operable	107	0.9	2.8	7.5	18.7	12.1	25.2	22.4	9.3
Inoperable	150	4.0	2.0	8.7	18.0	24.6	26.6	14.6	1.3
Body:									
Operable	26	0.0	0.0	11.5	3.8	34.6	34.6	11.5	3.8
Inoperable	75	2.7	6.7	5.3	10.6	13.3	49.4	10.6	1.3
Cardia:									
Operable	29	0.0	0.0	10.0	17.3	8.3	17.3	33.5	16.7
Inoperable	154	0.0	2.6	1.9	8.5	22.0	37.0	26.6	1.3
Extensive:									
Operable	51	2.0	0.0	16.0	6.0	20.0	29.0	16.0	10.0
Inoperable	252	0.8	2.0	5.6	13.9	15.8	31.7	20.6	9.5

In patients with gastric cancer and normochromic anemia, Rasmussen, Abels, Pack and Rhoads[20] found that forced protein feedings produced considerable nitrogen retention with plasma protein fabrication but without proportionate simultaneous production of hemoglobin, which suggests that there exists a disturbance in hemoglobin synthesis in patients with gastric cancer. Studies in the Memorial Hospital indicate that the macrocytic and normochromic anemia of these patients may not be on the same basis as that of pernicious anemia but is probably related to the associated hepatic insufficiency so commonly found in patients with gastric cancer. The two hematologic disorders pernicious anemia and the macrocytic anemia of gastric cancer differ in several ways:

20. Rasmussen, L. H.; Abels, J. C.; Pack, G. T., and Rhoads, C. P.: Metabolic Studies on Patients with Cancer of the Gastro-Intestinal Tract: XIV. The Effects of High Protein Diets on the Prevention of Postoperative Hypoproteinemia in Patients with Gastric Cancer, J. A. M. A. **124**:358-360 (Feb. 5) 1944.

1. In pernicious anemia the macrocytosis is uniformly associated with hyperchromia; in gastric cancer the macrocytosis is uniformly normochromic.

2. Only 1 of 25 patients with gastric cancer and macrocytosis had leukopenia or lymphocytosis; yet these conditions occur frequently in cases of pernicious anemia in relapse.

3. In 10 patients with gastric carcinoma and macrocytic anemia the marrow count did not show the impaired maturation of erythroblasts so characteristic of pernicious anemia.

4. The intramuscular injection of liver extract uniformly elicits a reticulocyte response in patients with pernicious anemia; the daily parenteral administration of 30 to 45 units of antianemia principle for fourteen to eighteen days to patients with gastric cancer and macrocytic anemia did not induce significant reticulocytosis.

5. Achlorhydria is a constant feature of pernicious anemia; this condition occurred even less frequently in patients with gastric cancer and macrocytosis than it did in patients with either normocytosis or microcytosis.

Much has been written about the relationship of carcinoma to pernicious anemia, but it will suffice here to state that among more than 1,000 patients with gastric cancer seen at the Memorial Hospital only 1 patient with an established diagnosis of pernicious anemia has been encountered. Pernicious-like anemias have been seen in patients who have been proved to have multiple bone metastasis (myelophthisic anemia).

Although the presence or degree of anemia is of no prognostic importance as far as the resectability of a gastric cancer is concerned, it is, of course, a real factor in the operative mortality and should be corrected, if possible, so that a hemoglobin level of at least 70 per cent (10.5 Gm.) is present before surgical intervention is undertaken. The preoperative administration of whole blood induces a relatively high incidence of febrile reactions and intravascular lysis. Nevertheless, the patients scheduled for gastrectomy should have their proper quota of transfusions inasmuch as anemia increases their tendency to shock and their susceptibility to infection, aggravates their usual hypoproteinemia, impairs wound healing and predisposes to wound disruption.

ROENTGENOLOGIC AND GASTROSCOPIC DIAGNOSIS OF GASTRIC CANCER

The results of roentgenologic and gastroscopic studies are presented to emphasize their importance individually and jointly as the most reliable means of establishing the diagnosis of gastric carcinoma. We

do not intend to contrast the accuracy of one procedure as opposed to the other but wish to emphasize that no diagnostic study should be neglected in ruling on the diagnosis of gastric cancer in any person who could be suspected of having this disease.

The roentgenologist made an unequivocal diagnosis of changes compatible with gastric cancer in 91.5 per cent of 1,022 patients who had a series of gastrointestinal roentgenograms made at the Memorial Hospital. In an additional 31 patients (3 per cent) an inconclusive diagnosis was made. By this we mean that the presence of cardioesophageal or pyloric obstruction was detected in 26 patients and of a "questionable" lesion in 5 patients. For 56 (5.5 per cent) of the patients a report of findings within normal limits was made; in these cases the diagnosis was subsequently established by gastroscopy or at operation. In the following discussion of gastroscopic studies the incidence of roentgen-positive diagnoses averages somewhat below 91.5 per cent, but this is due to the fact that in all cases in which any doubt of the diagnosis was entertained gastroscopy was performed.

Three hundred and five patients were given both gastroscopic and roentgenologic examination. In 161 the open tube gastroscope was used and in 144 the flexible one. Since 1940 the open tube gastroscope has been limited to the study of lesions believed to involve the cardia of the stomach and/or the lower end of the esophagus. Prior to this time the gastroscopist was called on to judge whether the proximal level of the cancerous involvement of the stomach precluded resection. Since then technics have been developed for total abdominal or transthoracic gastrectomy. The flexible gastroscope is employed in searching for all other gastric lesions. The use of the open tube instrument demands considerable skill, but the findings are relatively easy to interpret. The flexible gastroscope, however, is not too difficult to pass, but considerable experience is required in interpreting what is visualized.

In table 8 the diagnoses made in the 305 patients in whom both roentgenologic and gastroscopic studies were done are compared. The data are presented in three columns; these cover, from left to right, patients in whom both methods of gastroscopy were used, patients in whom only the open tube gastroscopy was used and those in whom the flexible gastroscope was used.

Among the 161 patients in whom the open tube gastroscopy was used a positive diagnosis was made roentgenologically in 85.1 per cent and gastroscopically in 71.4 per cent, with agreement by both methods in 60.2 per cent. The roentgenogram of 1 patient was interpreted as normal but a positive diagnosis was made on gastroscopic examination. In 25 patients, or 15.5 per cent, the results of gastroscopy were negative

but the roentgenograms revealed the disease. In 15, or 9.3 per cent, the results of roentgenologic examination were positive and those of gastroscopy inconclusive, and in 17, or 10.6 per cent, the roentgen study was inconclusive and gastroscopic study gave positive results. By both methods either a positive or an inconclusive diagnosis was always made. When gastroscopy was employed, the incidence of positive diagnosis was increased from 85.1 (roentgenologic study alone) to 96.3 per cent and that of suspected cancer (inconclusive diagnosis) increased to 100 per cent. Other combinations of positive, inconclusive and negative diag-

TABLE 8.—*Diagnosis of Gastric Cancer by Gastroscopic and Roentgenologic Study**

Method or Combination of Methods Used in Making the Diagnosis	Total Cases		Open Tube Gastroscope		Flexible Gastroscope	
	No.	%	No.	%	No.	%
Total number of cases	305	100.0	161	100.0	144	100.0
Positive diagnosis by gastroscopic and roentgenologic study	294	96.4	155	96.3	139	96.5
Positive diagnosis, agreement by both methods	207	67.9	97	60.2	110	76.4
Positive diagnosis by roentgen examination	265	86.9	137	85.1	128	88.9
Inconclusive diagnosis by roentgen examination	36	11.8	23	14.3	13	9.0
Negative diagnosis by roentgen examination	4	1.3	1	0.6	3	2.1
Positive diagnosis by gastroscopy	236	77.4	115	71.4	121	84.0
Inconclusive diagnosis by gastroscopy	32	10.5	16	9.9	16	11.1
Negative diagnosis by gastroscopy	37	12.1	30	18.6	7	4.9
Positive diagnosis by gastroscopy, negative by roentgen examination	3	1.0	1	0.6	2	1.4
Positive diagnosis by gastroscopy, inconclusive by roentgen examination	26	8.5	17	10.6	9	6.3
Positive diagnosis by roentgen examination, negative by gastroscopy	29	9.5	25	15.5	4	2.8
Positive diagnosis by roentgen examination, inconclusive by gastroscopy	29	9.5	15	9.3	14	9.7
Inconclusive diagnosis by gastroscopy and roentgen examination	3	1.0	1	0.6	2	1.4
Inconclusive diagnosis by roentgen examination, negative by gastroscopy	7	2.3	5	3.1	2	1.4
Negative diagnosis by gastroscopy and roentgen examination	1	0.3	0	0.0	1	0.7

* This table presents the combinations of positive, inconclusive and negative diagnoses made in 305 patients who had both gastroscopic and roentgenologic studies. The results are tabulated for the total number of patients, for those in whom open tube gastroscopy was performed and for those in whom flexible gastroscopy was performed.

noses by the two methods alone and together are given in the table but are not discussed.

It is perhaps significant that in 71.4 per cent of the cases of accessible lesions biopsy of material obtained through the open tube gastroscope revealed the disease. In 3 instances positive results of biopsy were obtained in patients who had irregularities of an uncertain nature roentgenologically, and in 1 case biopsy revealed the disease when a series of gastrointestinal roentgenograms was interpreted as showing a normal condition. The roentgenologist was unable to differentiate between carcinoma of the lower end of the esophagus and cardiospasm in 9 patients; biopsy of material obtained by gastroscopy showed the presence of car-

cinoma. This is a not infrequent error in diagnosis, and since many such lesions are resectable every possible means must be employed to discover their presence at an early stage.

Among 144 patients in whom gastroscopy was performed with the flexible instrument a positive diagnosis was made gastroscopically in 84 per cent, roentgenologically in 88.9 per cent and by both methods in 76.4 per cent. In 2 patients roentgen examination gave negative results but gastroscopic study revealed the presence of cancer. In 9, or 6.3 per cent, of the patients gastroscopy gave positive results and roentgen study was inconclusive, and in 14, or 9.7 per cent, roentgen examination yielded positive results but gastroscopy was inconclusive. A positive diagnosis by both methods was made in 139 patients, or 96.5 per cent, and with the addition of the inconclusive data the incidence of cases in which cancer was suspected was raised to 99.3 per cent. Thus by use of the flexible gastroscope the incidence of positive preoperative diagnosis has been increased from 88.9 per cent (roentgen study alone) to 96.5 per cent, an increase of 7.6 per cent.

When the data are combined for the 305 patients, the incidence of positive diagnosis is raised from 86.9 per cent by roentgenologic study to 96.4 per cent when gastroscopy was used. A positive diagnosis on gastroscopy was obtained in 77.4 per cent, on roentgenologic study in 86.9 per cent and by both methods in 67.9 per cent. In 3 cases the roentgen diagnosis was negative but gastroscopy revealed the presence of cancer. In 26, or 8.5 per cent, gastroscopy gave positive results and roentgen study was inconclusive, and in 29, or 9.5 per cent, roentgen study showed positive results but gastroscopy was inconclusive. A positive diagnosis was made from both roentgenograms and gastroscopy in 96.4 per cent, and with the addition of the inconclusive data the incidence of the probable presence of cancer of the stomach is raised to 99.7 per cent. The gastroscope allows the clinician to increase his preoperative diagnostic acumen 12.8 per cent, which must be considered important enough to demand gastroscopic examination of any patient for whom the diagnosis of cancer of the stomach is doubtful.

To recapitulate, for 10, or 3.3 per cent, of this group of 305 patients no definite diagnosis was made by either method. There were completely negative reports by both methods in 1 case; an abnormality not stated to be consistent with cancer was found on roentgen examination in 7 patients and on gastroscopic study in 3 patients.

Among the 305 patients for whom both a series of gastrointestinal roentgenograms and gastroscopic examination were used a positive diagnosis was made for 96.4 per cent, with abnormalities being present in 3.3 per cent. For 0.3 per cent of these patients there was a report of "essentially normal" findings by both methods, a fact which indicates the importance of the diagnostician's insistence on an exploration,

despite negative results of a battery of ancillary studies, of any patient whose history and symptoms are consistent with the probability of cancer of the stomach. Thus the clinician achieves an incidence of positive diagnosis of 100 per cent, confirmed by roentgenologic and/or gastroscopic study in 96.4 per cent of the cases. With advances in roentgenologic and gastroscopic technics, this small gap may eventually be closed. No one, however, should be subjected to laparotomy without first having had a roentgenologic examination of the gastrointestinal tract by a competent roentgenologist and a gastroscopic examination by an experienced gastroscopist. The proper sequence, of course, is to complete the roentgen examination (including fluoroscopy) first before doing gastroscopy. The gastroscope should never be passed until a preliminary roentgen study reveals the absence of an obstructive lesion involving the cardiac orifice.

The cause of certain gastric ulcerations has proved a stumbling block to clinicians inasmuch as gross pathologic interpretation is by no means infallible. As a result, one would anticipate a similar difficulty confronting the gastroscopist. When the ulceration proved to be cancerous, review of the preoperative interpretations suggested a high degree of accuracy after visualization of the lesion. It is in the study of the supposed peptic ulceration that the greatest number of pitfalls lie. Fifty-two patients underwent subtotal gastrectomy or gastrotomy with excision for peptic ulcer at the Memorial Hospital. Analysis of the preoperative examination is as follows:

Correct roentgenologic interpretation	23
Incorrect roentgenologic interpretation	15
Inconclusive roentgenologic interpretation	12
Inadequate data	2

Hence for only 46 per cent of 50 patients undergoing laparotomy was an accurate preoperative roentgen diagnosis obtained.

The record of the gastroscopist at the Memorial Hospital is still less satisfactory. Among the 52 patients, gastroscopic examination was carried out in 30, with the following result:

Correct gastroscopic interpretation	6
Incorrect gastroscopic interpretation	12
Inconclusive gastroscopic interpretation	12

If considered from a competitive point of view, the gastroscopist suffers greatly by comparison, but if the clinician is solely interested in accurate diagnosis and not the method employed, he should be extremely gratified that in 6 additional instances he was warned of the malignant nature of the gastric ulcerations in question. Until specimens can be removed for pathologic study through the flexible gastroscope, the cause of many gastric ulcerations doubtless will remain obscure.

SUMMARY AND CONCLUSIONS

Symptomatology and Physical Findings.—1. An analysis of the symptomatology, physical findings, gastric analyses and hematologic, roentgenologic and gastroscopic studies of 1,117 patients with gastric carcinoma is presented.

2. The frequency and multiplicity of symptoms in patients with inoperable and operable gastric cancer was essentially the same with the exception of dysphagia, which was twice as common among patients with inoperable carcinoma.

3. The resectability rate for carcinoma involving the cardia of the stomach was 20 per cent greater than that for carcinoma involving the stomach as a whole.

4. The symptoms presented by these patients, in decreasing order of frequency, were loss of weight, pain, vomiting, disturbances of the bowel, anorexia, dysphagia, nausea, weakness, eructation, hematemesis and rapid satiation.

5. Loss of weight above 41 pounds (18.6 Kg.) was usually associated with gastric cancer in an inoperable stage. The rapidity of the loss as well as the percentage is more important than the absolute fall in poundage.

6. Pain, dysphagia and anorexia were among the first definitive complaints of the patients studied.

7. Dysphagia was the first symptom experienced in 40 per cent of the patients with involvement of the cardia.

8. Pain occurred more commonly with cancers involving the lesser curvature of the body of the stomach. Pain caused by cancers of the cardia may simulate angina pectoris.

9. Anorexia was more frequent with pyloric and prepyloric cancers.

10. The duration of symptoms bore no relation to the resectability of the lesion.

11. The surgical mortality was more than three times as great among the patients whose symptoms had been present from eighteen to thirty-six months as among those whose complaints were of shorter duration.

12. Of 155 patients who had gastrointestinal symptoms for more than two years, 53 gave a history of ulcer-like pain and 102 had complained of vague indigestion. In a large majority of the patients a change in symptoms developed that could have been an important clinical clue to the development of carcinoma of the stomach.

13. Mass roentgenologic studies do lead to early recognition of gastric cancer in from 0.2 to 0.5 per cent of persons without gastric complaint but, at present, are economically impractical.

14. An epigastric mass was palpable in 57 per cent of the patients with inoperable and 42 per cent of the patients with operable gastric cancers. Such a finding does not, therefore, indicate inoperability.

15. Aspiration biopsy of the liver is justifiable when this organ is large and nodular. Peritoneoscopy should be employed when one suspects peritoneal carcinosis or hepatic metastasis. Positive findings in either procedure interdict exploratory laparotomy unless palliative procedures are planned.

16. On the basis of the physical findings alone, 11 per cent had one or more signs indicating the inoperable nature of the cancer, i. e., signal nodes, Blumer's shelf, ascites, jaundice, obviously nodular liver or other pelvic implants.

Laboratory Studies.—1. Achlorhydria was present in 65.0 per cent of the patients with inoperable gastric cancer and in 51.1 per cent of those whose carcinomas were resected.

2. Extensive carcinoma of the stomach was associated with a 10 per cent increase in achlorhydria over that found in the group as a whole.

3. Anacidity was 15 per cent greater in cases of grade IV anaplastic carcinoma than in instances of less malignant tumors.

4. The incidence of achlorhydria increased in proportion to the size of the tumor.

5. Excessive amounts of free hydrochloric acid were encountered twice as frequently in patients with benign gastric ulcer as in patients with gastric cancer and three times as often as in normal adults 60 to 64 years of age.

6. Low acidity occurs in the same proportion in normal persons 60 to 64 years of age, in patients with gastric cancer and in patients with benign gastric ulcer.

7. The degree of anacidity encountered in older age groups gives no definite clue to the presence or absence of cancer.

8. A relatively high degree of achlorhydria was found among patients with polypoid gastric cancers and infiltrating gastric carcinomas.

9. Studies of the gastric juice for cancer cells by the Papanicolaou technic offers an important additional diagnostic aid.

10. The degree of anemia bore no relation to the segmental location of the gastric cancer or to its resectability.

11. No correlation was found between the degree or type of anemia and the incidence of achlorhydria.

12. The microcytic anemia of gastric cancer does not respond well to iron therapy.

13. The macrocytic anemia of gastric cancer is nearly always normochromic. It simulates pernicious anemia but lacks many of its distinguishing hematologic characteristics.

Roentgenologic and Gastroscopic Diagnosis.—1. On the basis of 1,022 gastrointestinal studies positive diagnosis of gastric cancer was made in 91.5 per cent of patients and inconclusive diagnosis in 3 per cent, with findings reported within normal limits in 5.5 per cent.

2. By use of the open tube gastroscope in 161 patients positive evidence of gastric cancer was obtained in 71.4 per cent, inconclusive evidence in 9.9 per cent and negative results in 18.6 per cent. In these same patients positive diagnosis was made by roentgenologic study in 85.1 per cent, inconclusive diagnosis in 14.3 per cent and negative diagnosis in 0.6 per cent. Confirmative diagnosis in the same patients by both gastroscopic and roentgenologic study was obtained in only 60.2 per cent. By the employment of both methods the incidence of positive diagnosis was increased from 85.1 per cent by roentgen examination alone to 96.3 per cent. Positive results of biopsy of material obtained through the open tube gastroscope were secured in 71.4 per cent of the patients with accessible lesions.

3. Examination with the flexible gastroscope in 144 patients gave positive evidence of cancer in 84.0 per cent and inconclusive evidence in 11.1 per cent and was reported as showing no evidence of abnormality in 4.9 per cent. Results of roentgen examination were positive for 88.9 per cent of these patients and inconclusive for 9.0 per cent and were reported as within normal limits for 2.1 per cent. Gastroscopic and roentgenologic study of the same patients was confirmative in 76.4 per cent. The incidence of positive diagnosis obtained by the use of both methods was 96.5 per cent, an increase of 7.6 per cent over the 88.9 per cent incidence of positive diagnosis obtained by roentgen examination alone.

4. Among 305 patients who had both roentgenologic and gastroscopic examination the use of the gastroscope raised the incidence of positive preoperative diagnosis 9.5 per cent.

5. Abnormalities detected in roentgenograms and/or gastroscopy and not considered diagnostic of cancer were found in an additional 3.3 per cent of the 305 patients, raising the probability of the presence of cancer of the stomach to 99.7 per cent.

6. No patient with persistent symptoms indicative of gastric cancer should be denied exploration even in the face of negative results from a battery of ancillary studies.

MODIFICATION OF COOPER'S LIGAMENT HERNIORRHAPHY USING HALSTED'S FASCIAL FLAP

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KANSAS CITY, KAN.

ANSON and McVey [1] in 1938 made what is probably the most outstanding contribution in the past twenty-five years to our understanding of the anatomy of the inguinal region. A more anatomic inguinal herniorrhaphy was recommended by McVey in 1941.[2] This repair utilized the ligamentum pubicum superius, or Cooper's ligament, instead of the inguinal ligament, which is justified by the fact that Cooper's ligament is the normal insertion of the musculus et aponeurosis transversus abdominis.

Exclusive of its anatomic character, the McVey herniorrhaphy has the advantage of being applicable to the repair of a direct or indirect inguinal hernia or a femoral hernia. It may be used also to close any hernia which is a combination of these two, the Hoguet maneuver being employed to convert two sacs into one. The disadvantages are generally those of difficult dissection and exposure, due to the depth of the wound, excessive tension on the conjoined tendon and a potential dead space in the area under the spermatic cord.

The first disadvantage may be overcome by adequate retraction at operation plus the use of the Davis tonsil needle for placing the sutures through the conjoined tendon and Cooper's ligament. This needle is of heavy gage stock but has a short length and bite. It has been found that in the treatment of a hernia on the right side it is advisable to place the suture first through Cooper's ligament, the point of the needle in its holder being directed away from the surgeon, while retracting the femoral vessels laterally with a retractor or an index finger. If the needle is passed through Cooper's ligament in a direction toward the operator, there is a marked tendency for the point to swivel toward the femoral vein, making it difficult to control. Of course this principle would also be applicable when a left-handed surgeon is repairing a hernia on the left side.

From the Surgical Service of the University of Kansas Medical Center.

1. Anson, B. J., and McVey, C. B.: The Anatomy of the Inguinal and Hypogastric Regions of the Abdominal Wall, Anat. Rec. **70**:211, 1938.

2. McVey, C. B.: An Anatomic Error in Current Methods of Inguinal Herniorrhaphy, Ann. Surg. **113**:4, 1941.

The answer to the problem of tension has been given by Halsted [3] and more recently by Rienhoff.[4] They recommended a longitudinal incision through the rectus fascia to provide relaxation of the conjoined tendon. Halsted also used a triangular flap of rectus fascia which he turned down and sutured to Poupart's ligament to reinforce the hernial closure.

In 1946 Mattson [5] suggested approximating the Halsted flap of fascia to Cooper's ligament, his idea being to apply the technic especially for direct and recurrent inguinal hernias or when a weak conjoined tendon is found. Mattson's technic may also be useful in persons in

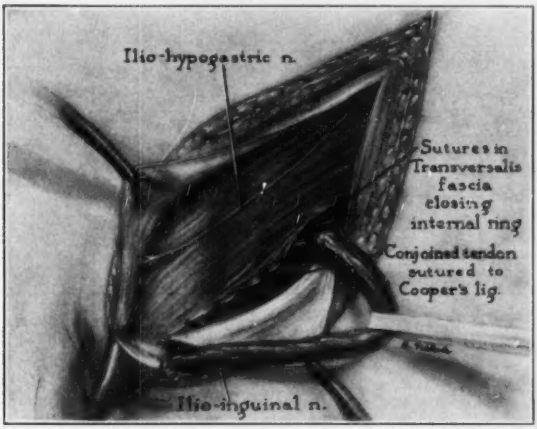
Ilio-hypogastric n.
Sutures in Transversalis fascia closing internal ring
Conjoined tendon sutured to Cooper's lig.
Ilio-inguinal n.

Fig. 1.—Reconstruction of the abdominal wall utilizing Cooper's ligament.

whom muscularity is such that to bring down the conjoined tendon to Cooper's ligament might cause excessive tension.

The modification here presented not only solves the problem of relaxation with Halsted's and Rienhoff's relaxing incision but obliterates the dead space under the spermatic cord by suturing the rectus flap to Poupart's ligament after anchoring the conjoined tendon to Cooper's

3. Halsted, W. S.: The Cure of the More Difficult as Well as the Simpler Inguinal Ruptures, Bull. Johns Hopkins Hosp. **14**:208, 1903.

4. Rienhoff, W. F.: The Use of the Rectus Fascia for Closure of the Lower or Critical Angle of the Wound in Repair of Inguinal Hernia, Surgery **8**:326, 1940.

5. Mattson, H.: Use of Rectus Sheath and Superior Pubic Ligament in Direct and Recurrent Inguinal Hernia, Surgery **19**:498, 1946.

ligament (figs. 1 and 2). The longitudinal incision through the rectus sheath is made as medial as is practicable to provide a long mobile flap of fascia. This flap is sutured to the inguinal ligament under the spermatic cord rather than superficially as originally described by Halsted. The use of this flap adds strength to the hernial repair.

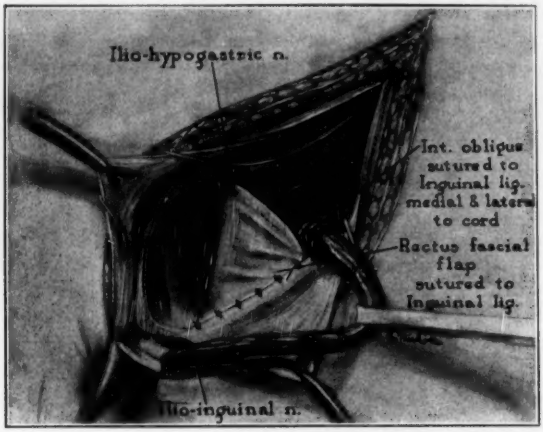
Ilio-hypogastric n.
Int. oblique sutured to Inguinal lig. medial & later to cord
Rectus fascial flap sutured to Inguinal lig.
Ilio-inguinal n.

Fig. 2.—Use of rectus fascial flap to reinforce Cooper's ligament herniorrhaphy.

SUMMARY

The advantages and disadvantages of the McVey type of herniorrhaphy are mentioned. Two of the chief disadvantages are tension and the retrocordal dead space.

A method of overcoming these disadvantages is presented. In addition to a relaxing incision through the rectus fascia, a fascial flap is constructed and sutured to the inguinal ligament under the cord, aiding in the closure of the dead space and adding a second line of defense in the reconstruction of the abdominal wall.

MESENTERIC VASCULAR OCCLUSION

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AND
JACK LASNER, M.D.
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IT IS NOW one hundred and five years since Tiedemann reported the first case of mesenteric vascular occlusion. Virchow described the disease in detail in 1847. The total number of reported cases is near 900. Elliot first operated successfully for mesenteric vascular occlusion in 1895. In 1921 Klein recorded 24 cases of successful resection. In 1931 Meyer added 14 cases in which the patient survived resection. Since 1931, 25 patients who survived resection, including the one presented in this paper, have been reported on. This brings the total of successful resections to 63.

Mesenteric vascular occlusion is one of the most fatal of all abdominal conditions. This condition masquerades well and is difficult of recognition. It is relatively rare, and few cases are observed by any one surgeon.

A survey of the records from the Massachusetts General Hospital by Warren and Eberhard revealed that occlusion of mesenteric vessels was encountered in 13 of 48,000 patients with surgical conditions admitted to the hospital. The incidence at Touro Infirmary, New Orleans, from 1938 to 1947 was 19 cases among 55,232 surgical cases.

The mortality rate for the disease varies, but it is conceded as ranging from 60 to 90 per cent. Warren and Eberhard reviewed 75 cases and found that when exploration was not done the mortality rate was 95 per cent. In cases in which resection was done the mortality rate was 34.2 per cent.

In 1931 Meyer reviewed 92 proved cases of mesenteric vascular occlusion over a ten year period. He found a mortality rate of 32.6 per cent among 43 patients operated on. This is by far the lowest mortality rate of any reported series. A review of the recent literature reveals the following operative mortality rates: Whittaker and Pemberton, 84 per cent in 19 patients operated on; Moore, 60 per cent in 7 patients; Ficarra, 63 per cent in 15 patients; St. Luke's Hospital, 86 per cent in 7 patients. The average mortality rate of these series is 72 per cent in 57 patients operated on.

We are presenting a case in which operation was performed successfully.

Read at the meeting of the Chicago Surgical Society on Jan. 2, 1948, Chicago.

From the departments of surgery, St. Luke's Hospital and the University of Illinois College of Medicine.

REPORT OF A CASE

A 53 year old white man entered St. Luke's Hospital on Dec. 16, 1940. He complained of abdominal pain, generalized in character and continuous in nature, of seven days' duration. There was no relationship between the pain and the intake of food or liquids. It did not radiate and was centered about the mid-abdomen. There was no nausea, vomiting, tenderness or distention. Bowel movements had been normal in color and consistency and occurred once daily. The past history revealed that the patient had several attacks of phlebitis of the left leg. These attacks were at intervals of three to six weeks and subsided when he rested in bed for a few days.

Physical examination revealed a well developed and well nourished white man of about 50 years of age. His blood pressure was 136 systolic and 84 diastolic. The pulse rate was 80. The oral temperature was 98.4 F.

The laboratory studies revealed the urine to contain 15 mg. of albumin per hundred cubic centimeters. The red blood cells numbered 3,780,000 per cubic millimeter. The leukocytes numbered 10,500 per cubic millimeter. The hemoglobin content was 11.6 Gm. per hundred cubic centimeters. The differential count revealed 82 neutrophils per hundred cells. Culture of a specimen of the stool revealed no growth after seventy-two hours. Chemical examination of the blood revealed the following: The urea nitrogen was 27.5 per hundred cubic centimeters, the nonprotein nitrogen 50 mg., the alkali reserve 56.7 volumes per cent and the total serum protein 6 Gm. per hundred cubic centimeters.

A flat plate of the abdomen was normal. Roentgenologic studies of the chest revealed no abnormalities.

The patient was given sulfathiazole, and a tentative diagnosis of diverticulitis was made. The rectal temperature fluctuated between 100 and 101 F. The pulse rate was 90 to 100. The leukocytes increased to 16,800. Five days after his admission, the patient experienced severe and excruciating pain in the lower left region of the abdomen. The abdomen became tense and tender. No peristaltic sounds could be heard. Because of the obscure nature of the findings, abdominal exploration was recommended. A preoperative diagnosis of mesenteric vascular occlusion was made.

Operation.—Under ethylene anesthesia, an upper midline incision was made. When the peritoneum was opened, about 1,000 cc. of thin blood-tinged fluid escaped. A gangrenous loop of the upper area of the ileum was present. Distal to the gangrenous area, the ileum was collapsed. Resection of the gangrenous loop and the underlying mesentery was carried out and an end to end anastomosis accomplished. A Witzel ileostomy was performed proximal to the anastomosis. A total of 60 cm. of ileum was resected. The patient was given heparin. The postoperative course was uneventful for forty days. On the fortieth day the rectal temperature rose to 104 F. The leukocytes numbered 24,000. The patient appeared critically ill. The abdomen was markedly tender about the incision.

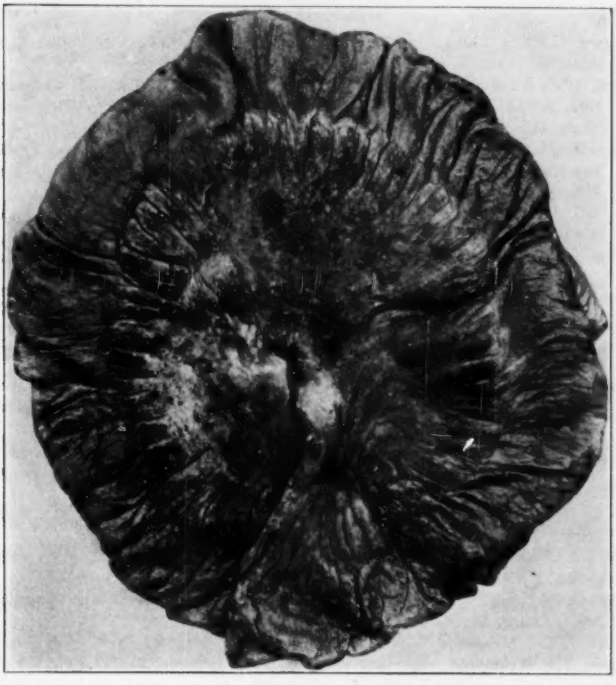
The abdomen was reexplored on the fortieth postoperative day. There was a large amount (3,000 cc.) of thin bloody fluid which escaped when it was opened. A loop of gangrenous ileum, distal to the previous area of resection, was present. Forty centimeters of ileum and mesentery was resected and an end to end anastomosis accomplished. A Witzel type of ileostomy was performed proximal to the anastomosis. The patient's postoperative course was uneventful. Heparin was not used. He was discharged forty-five days after the second operation.

At the present time he is well and carrying on an active business life.

Pathologic Report.—The report of the first resection, on Dec. 22, 1940, was as follows: "Mesenteric vein thrombosis and hemorrhagic necrosis of the small

bowel are present. When the bowel is opened lengthwise along its mesentery, there is, toward the hemorrhagic portion, pronounced edema. The lumen contains blood. In the hemorrhagic portion there are marked edema and extravasation of blood into the wall. The thickness of the wall approaches a maximum of 0.8 cm. In the hemorrhagic segment the surface mucosa is ulcerated in many places (see photograph).

The venous channels are markedly dilated and are filled with red blood cells, including a large number of polynuclear leukocytes. There is a notable amount



Photograph of small bowel resected at first operation, Dec. 22, 1940. This segment of bowel measured 60 cm.

of necrosis, edema and extravasation of red blood cells. The necrosis involves all layers of the wall of the bowel."

The second resection, on Jan 30, 1941, was reported as follows: "Mesenteric vein thrombosis and hemorrhagic necrosis of small bowel are present. At each end it is gray, moderately hyperemic and slightly edematous. In the mesentery opposite the hemorrhagic portion are small blood vessels distended with blood clots. The wall here is 0.7 cm. thick.

The blood vessels included are chiefly vein structures and the lumens of some of these are dilated with blood clots, masses of red blood cells with threads of fibrin and variably with polymorphonuclear leukocytes. The arteries contain blood

cells and also fibrin with leukocytes. The mucosa has extensive hemorrhages. In the muscularis are exudates of polymorphonuclear leukocytes. The subserous tissues are edematous and markedly infiltrated with leukocytes. There are fibrinous and leukocytic exudates on the peritoneum."

With the addition of the present case, 63 cases of successful resection for mesenteric vascular occlusion have been reported.

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RETROPERITONEAL FATTY TUMORS

Report of a Case and Collective Review of the Literature from 1937 to 1947

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FIFTY-TWO cases of benign and malignant fatty tumors of the retroperitoneal space were reported in the literature from 1937 to 1947.[1] The present case report makes this total 53. Von Wahlendorf.[2] collected 165 of such cases up to 1921. From 1921 to 1937, after all repetitions were deducted, it was estimated that 76 cases had been

1. (*a*) Bass, M. M.: Retroperitoneal Lipoma Simulating Ischiatic Hernia, Vestnik. khir. **56**:774, 1938. (*b*) Blue, J. H., and Lafferty, C. R.: Perirenal Lipoma, Surgery **6**:944, 1939. (*c*) Cattell, R. B., and Warren, K. W.: Retroperitoneal Lipoma, S. Clin. North America **27**:659, 1947. (*d*) Chown, B.: Extraperitoneal Lipoma in Child, Am. J. Dis. Child. **57**:401, 1939. (*e*) d'Agostino, M., and Sandrini, G.: Case of Retroperitoneal Lipoma and Pararenal Lipoma, Clinica **6**:503, 1940. (*f*) Flynn, J. M.: Retroperitoneal Liposarcoma with Myxomatous Degeneration, Radiology **35**:90, 1940. (*g*) Frank, R. T.: Primary Retroperitoneal Tumors, Surgery **4**:562, 1938. (*h*) Kretschmer, H. L.: Retroperitoneal Lipo-Fibro-Sarcoma in a Child, J. Urol. **43**:61, 1940. (*i*) Livermore, G. R.: Retroperitoneal Tumor Displacing Left Kidney, Tr. Am. A. Genito-Urin. Surgeons **31**:29, 1938. (*j*) Most, A.: Retroperitoneal Tumors, Arch. f. klin. Chir. **189**:571, 1937. (*k*) McLaughlin, C. W., and Sharpe, J. C.: Malignant Fatty Tumors of Retroperitoneal Region, Am. J. Surg. **41**:512, 1938. (*l*) Minuzzi, P. G., and Torresi, S.: Large Perirenal Myxolipoma, Rev. argent de urol. **9**:285, 1940. (*m*) Moreland, R. B., and McNamara, W. L.: Liposarcoma, Arch. Surg. **45**:164 (July) 1942. (*n*) Odinov, D. E.: Removal of Massive Lipoma of Retroperitoneal Space, Novy. khir. arkhiv. **44**:62, 1939. (*o*) Donnelly, B. A.: Primary Retroperitoneal Tumors, Surg., Gynec. & Obst. **83**:705, 1946. (*p*) Pkhakadze, O. L.: Retroperitoneal Lipomas, Rad. med. **5**:16, 1940. (*q*) Regan, J. S.: Sanes, S., and MacCallum, J. D.: So-Called Retroperitoneal Lipoma, Ann. Surg. **117**:110, 1943. (*r*) Stout, A. P.: Liposarcoma: Malignant Tumor of Lipoblasts, ibid. **119**:86, 1944. (*s*) Stromme, W. B. and Stander, H. J.: Retroperitoneal Tumors Simulating Genital Tract Neoplasms, Am. J. Obst. & Gynec. **52**:456, 1946. (*t*) Tomada, M.: Recurrent Retroperitoneal Lipoma, Zentralbl. f. Chir. **64**:999, 1937. (*u*) Griep, K.: Retroperitoneal Fibrolipoma, ibid. **67**:120, 1940. (*v*) Gilturner, G.: Huge Retroperitoneal Lipoma, Rev. clin. españ. **1**:527, 1940. (*w*) Windholz, E.: Roentgen Diagnosis of Retroperitoneal Lipoma, Am. J. Roentgenol. **56**:594, 1946. (*x*) Nordland, M.: Tumors of the Retroperitoneal Spaces, Tr. West. S. A. **51**:324, 1942. (*y*) Acuff, H.: Retroperitoneal Tumors, South Surgeon **11**:200, 1942. (*z*) Ockuly, E. A., and Douglas, F. M.: Retroperitoneal Perirenal Lipomata, J. Urol. **37**: 619, 1937.

2. von Wahlendorf, L.: Ueber retroperitoneale Lipome, Arch. f. klin. Chir. **115**:751, 1921.

reported.[3] Therefore a total of approximately 300 cases have been reported up to the present time (table 1).

Moreland and McNamara [1m] found 3 retroperitoneal liposarcomas among 16,000 tumors of all kinds. Donnelly [10] collected 95 cases of primary retroperitoneal tumors at the University of Iowa Hospital during a period of twenty years. Two of these were fatty tumors, 1 of which was malignant. Stromme and Stander [18] at the New York Hospital found 12 retroperitoneal tumors in 13,113 gynecologic operations. One was a retroperitoneal lipoma.

These tumors are of particular interest to gynecologists, urologists and general surgeons, for they appear in the pelvis and the lumbar area and may often fill the entire intra-abdominal cavity. They are usually

TABLE 1.—*Reports of Retroperitoneal Fatty Tumors*

Year	No. of Cases Reported
To 1921	165
1921 to 1937	76
1937 to 1947	53
	294

reported because of their rarity, large size, diagnostic and surgical problems and the interesting pathologic changes such as those found in the following case.

REPORT OF A CASE

N. M., a white man 52 years old whose occupation was that of a beer garden manager, was seen for the first time on Feb. 8, 1947. His chief complaint was bloating after meals for the past nine months. He had always enjoyed good

3. (*a*) Pemberton, J. DeJ., and McCaughan, J. M.: Intrarenal and Peri-Renal Lipomata, Surg., Gynec. & Obst. **56**:110, 1933. (*b*) Pemberton, J. DeJ., and Whitlock, M. D.: Large Retroperitoneal Lipoma, S. Clin. North America **14**: 601, 1934. (*c*) Williams, C.: Retroperitoneal Lipomyxosarcoma, J. A. M. A. **105**:195 (July 20) 1935. (*d*) Selman, W. A.: Report of a Case of Lipomyxosarcoma, Internat. Clin. **1**:136, 1931. (*e*) Andrews, E: Enormous Retroperitoneal Lipoma, S. Clin. North America **11**:105, 1931. (*f*) Bettman, R. B., and Greensfelder, L. A.: Retroperitoneal Lipoma, Surg., Gynec. & Obst. **37**:468, 1928. (*g*) Bettman, R. B., and Serby, J.: Retroperitoneal Lipoma, Arch. Surg. **24**: 300 (Feb.) 1932. (*h*) Burger, T. O.: Large Retroperitoneal Tumor, S. Clin. North America **7**:1285, 1927. (*i*) Mayo, C. H., and Dixon, C. F.: Retroperitoneal Lipoma, Minnesota Med. **10**:272, 1927. (*j*) Miller, J. R.: Retroperitoneal Pelvic Tumors Encountered by the Gynecologist, Am. J. Obst **32**:652, 1936. (*k*) Crabtree, E. G.: Perirenal Lipoma with Generalized Abdominal Lipomatosis, J. Urol. **23**:545, 1930. (*l*) Masson, J. C., and Horgan, E. T.: Retroperitoneal Lipomas, S. Clin. North America **1**:145, 1921. (*m*) Heppner, E.: Large Retroperitoneal Lipoma with Sarcomatous Degeneration, Ztschr. f. Urol. **14**:14, 1920. (*n*) Holmes, W. R.: Retroperitoneal Perirenal Lipomas, J. A. M. A. **75**:1065 (Oct. 6) 1920. (*o*) Hirsch, E. F., and Wells, H. G.: Retroperitoneal Liposarcoma, Am. J. M. Sc. **159**:356, 1920. Frank.[1g]

health, was athletically inclined and for years regularly attended a health club for exercise, swimming and massage. His abdomen had been large as long as he could remember, but he thought that it was getting larger during the past three to four years. In an attempt to reduce its size he exercised vigorously and masseurs gave him vigorous massages, pounded his abdomen and threw the medicine ball at it. About nine months previously he began complaining of pressure pains in the upper part of his abdomen, bloating and discomfort immediately after meals. This became progressively worse so that he was obliged to eat less and less food. During the previous six weeks he lost 10 pounds (4.5 Kg.) in weight, but he believed that his abdomen was getting larger. He became constipated and required laxatives about twice a week. Three months previously he had had two attacks of vomiting and diarrhea. Otherwise he has had no associated nausea, vomiting, belching or heartburn and had never been jaundiced. His stools had never been bloody, tarry or clay colored.

He had little knowledge of his family history but believed that two of his brothers died of "tumors." His personal habits were good. He had a wife and two children who were living and well.

Bilateral inguinal herniorrhaphy had been performed on Jan. 8, 1944. (His previous surgeon offered the information that many lipomas of various sizes were removed from the inguinal canals, the pathologic diagnosis of which was fibrolipoma.) During the past year there had been nocturia. Otherwise his past history was noncontributory.

The patient was a white man who was rather poorly nourished and appeared chronically ill. His weight was 170 pounds (77.3 Kg.). The blood pressure was 130 systolic and 80 diastolic. An enormous abdominal protrusion was seen when the patient was in the standing position. In the supine position this protrusion represented a large intra-abdominal mass about the size of a football, with the umbilicus approximately at its center. The upper border of the mass was felt about 7 cm. below the costal margin, and the lower margin reached below the level of the anterior-superior iliac spine. The diameter of the mass was approximately 25 cm. The mass felt firm and nodular, had an irregular surface and was not tender. There was no movement of the mass downward on deep inspiration. Ballottement with one hand in the lumbar area revealed an area of fulness there which was not movable. It felt slightly movable anteriorly, however. A fluid wave was not present, and it was doubtful whether there was shifting dulness.

A small soft mass, round, with a smooth surface, not tender and about 2 cm. in diameter, was present on the forehead above the right eye. It was fairly easily movable. A similar mass, about 4 cm. in diameter, was present in the subcutaneous tissue in the right lumbar region. Otherwise the physical examination was essentially noncontributory.

The urine was amber, clear and slightly acid and had a specific gravity of 1.020. Reactions to tests for albumin and sugar were negative, and the microscopic examination revealed an occasional white blood cell. The hemoglobin content was 82 per cent; the red blood cell count 4,200,000, and the white cell count 6,900, with 62 per cent neutrophils, 56 per cent filamentous forms and 6 per cent nonfilamentous forms, 6 per cent eosinophils and 32 per cent lymphocytes. Kahn and Wassermann reactions were negative. The blood nonprotein nitrogen level was 21.7 mg. per hundred cubic centimeters.

A series of roentgenograms of the gastrointestinal tract revealed the stomach to be high in position and transversely directed. The duodenum was normal except

for slight displacement of the fourth segment toward the right, and as the jejunum filled it was seen to be displaced entirely into the right side of the abdomen (fig. 1 *A*). At four hours the stomach was empty. There was normal distribution of barium through the small bowel. All segments of the small intestine lay well over on the right side and were somewhat higher than usual (fig. 1 *B*). The barium filled the colon readily and completely. There was displacement of the rectum, sigmoid and descending colon from the normal position

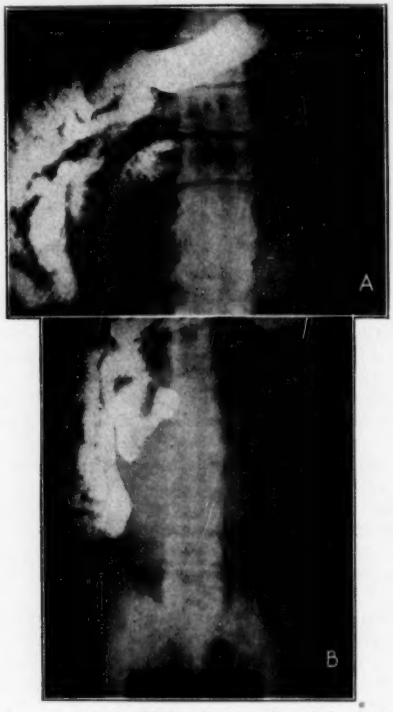

Fig. 1.—*A*, the stomach is displaced upward and is directed transversely. *B*, all segments of the small intestine lie well over on the right side and are somewhat higher than usual.

on the left entirely across the abdominal cavity to the right side, so that the descending and ascending portions of the colon lay in close proximity (fig. 2 *A*). A large mass on the left displaced the left side of the colon across the abdomen to the right.

In the roentgenogram of the chest the diaphragm occupied a high position because of the enlarged abdominal mass (fig. 2 *B*).

An intravenous pyelogram revealed deformity of the left pyelographic pattern, with lack of filling of the lower pole calices (fig. 3). There was no deformity of the renal pelvis or of the calices of the right kidney. The right ureter was demonstrated.

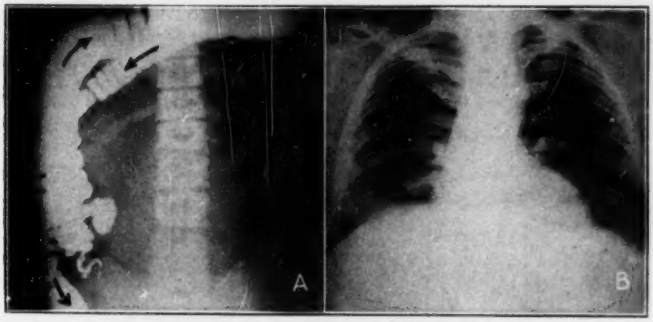

Fig. 2.—*A*, displacement of the rectum, sigmoid, and descending colon from the normal position on the left entirely across the abdominal cavity to the right side, so that the descending and ascending portions of the colon lie in close proximity. *B*, the diaphragm occupies a high position because of the enlarged abdominal mass.

Fig. 3.—Deformity of the left pyelographic pattern, with lack of filling of the lower pole calices.

The patient was admitted to Rogers Hospital on Feb. 21, 1947, and prepared for operation. The preoperative diagnosis was retroperitoneal tumor. The possi-

bility of retroperitoneal lipoma was considered in view of the presence of lipomas in the inguinal canals and the presence of lipomatosis (forehead and back).

A left rectus, muscle-splitting incision about 20 cm. long was made, with the level of the umbilicus as center. The tumor was retroperitoneal, the posterior peritoneum being in intimate contact with the parietal peritoneum of the anterior abdominal wall. It was much larger than was indicated by clinical examination, which necessitated lengthening the incision upward for 4 cm. and making another incision, perpendicular to the center of the original one, about 10 cm. long. This produced adequate exposure. The posterior peritoneum was carefully opened over the tumor on the left and then separated from it by both blunt and sharp dissection.

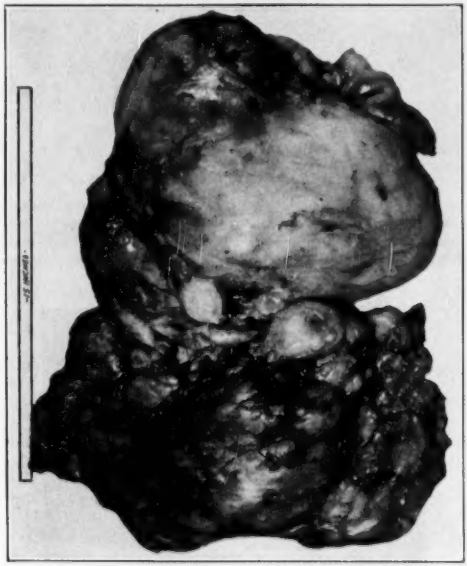

Fig. 4.—Two large masses, placed side by side, weighing 29 pounds (13.2 Kg.). They are encapsulated, and lobulated, yellowish in some areas and glistening white in others.

The tumor occupied the entire left side of the abdomen and about two thirds of the right side, extending from the diaphragm above to the pelvis below. The liver and gallbladder were displaced upward, the stomach was crowded upward and to the right and the left colon had been lifted from its normal position and displaced to the extreme right. The small intestine was crowded into a narrow space in the right upper quadrant. The consistency of the tumor varied; it felt firm to the touch in some areas and softer in others. The surface felt lobulated. Attempts at aspiration were unsuccessful. Most of the tumor was yellowish, with several whitish spherical areas varying from 3 to 8 cm. in diameter and much harder in consistency scattered throughout. These areas had a smooth glistening surface. The tumor was well encapsulated.

A transverse line of cleavage was found dividing it into approximately equal upper and lower halves. The lower half was removed first. The ureter was found coursing along the right edge of the lower half and was carefully separated from it by blunt dissection. The upper half was then removed. The tumor separated easily from the surrounding tissue; the mesenteric vessels were encountered, from which it was carefully separated. It was loosely adherent to the left kidney and was easily separated from it. The left kidney appeared smaller

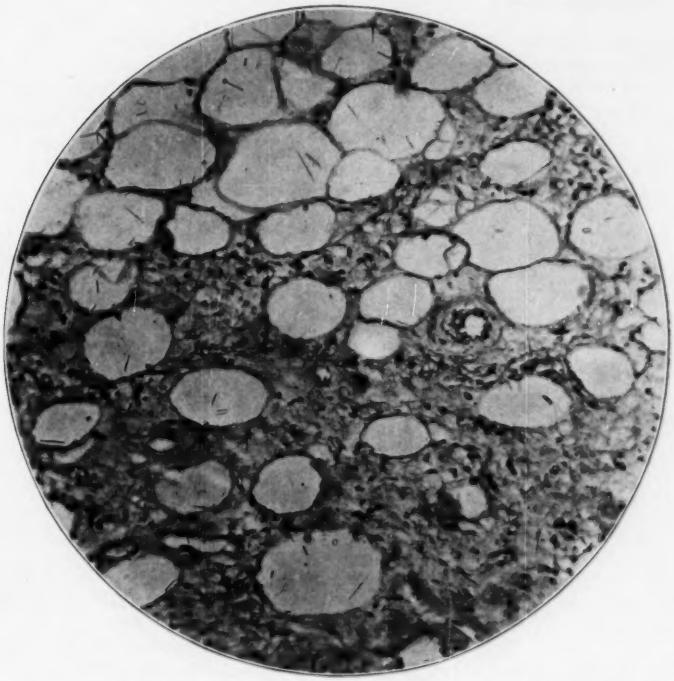

Fig. 5.—Myxomatous tissue infiltrating adipose tissue.

than normal and flattened out. Redundant posterior peritoneum was excised, and the descending colon was brought back over to its normal position on the left side and sutured in place. Two Penrose drains were inserted in the retroperitoneal space and brought out at the lateral end of the transverse incision.

During the operation the patient received 1,000 cc. of whole blood and 1,000 cc. of 5 per cent dextrose in isotonic sodium chloride solution. His condition was satisfactory until just before closure, when his blood pressure dropped from 120 systolic and 80 diastolic to 80 systolic and 60 diastolic. An ampul (0.1 Gm.) of metrazol® (pentamethylenetetrazol) was given. The blood pressure rose to

100 systolic and 80 diastolic, and at the termination of the operation it was 90 systolic and 60 diastolic. The pulse rate remained between 70 and 90 per minute throughout.

The pathologic tissue was studied by Dr. Clarence I. Owen, who reported the microscopic examination as follows: "The specimen is a new growth, weighing 29 pounds (13.2 Kg.) (fig. 4). It consists partly of adipose tissue (fig. 5) and partly of a myxomatous tissue which is widely infiltrating the former. The myxomatous portion of the new growth is composed of cells that vary considerably in size and staining qualities but that are, in general, stellate in shape with round or oval nuclei and long cytoplasmic processes (fig. 6). Most of the nuclei are fairly deeply stained, and there is a background of blue-staining material. The diagnosis is lipomyxosarcoma."

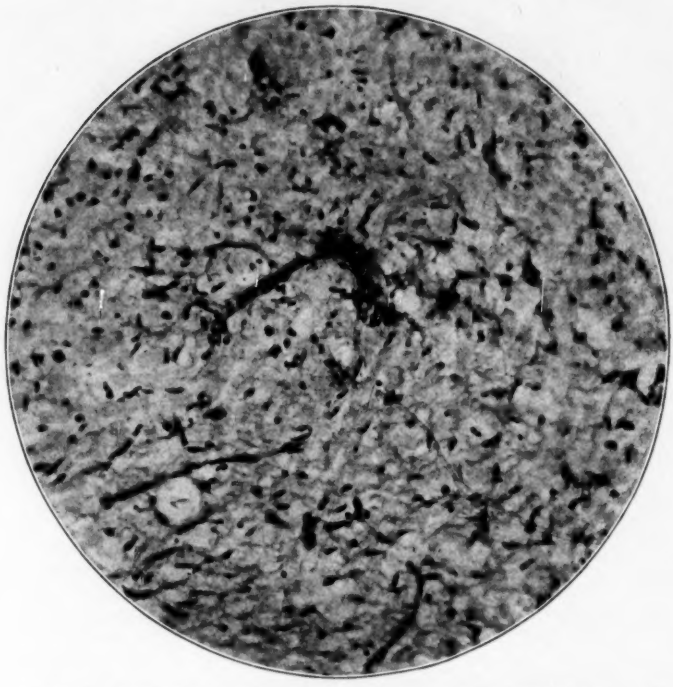

Fig. 6.—Myxomatous tissue composed of cells varying considerably in size and staining qualities but in general stellate in shape, with round or oval nuclei and long cytoplasmic processes. Most of the nuclei are fairly deeply stained.

The postoperative course was satisfactory. Five hundred cubic centimeters of blood plasma was given twelve hours after operation. Early ambulation was

attempted, but when the patient sat up on the first day his blood pressure dropped from 120 systolic and 80 diastolic to 70 systolic and 50 diastolic. On the second day after operation he was able to sit at the edge of the bed; the blood pressure was 130 systolic and 80 diastolic, and it remained constant thereafter. During the first six days he had considerable pain and difficulty in voiding and often required catheterization. Numerous pus cells were found in his urine. This finally necessitated the use of an indwelling catheter and daily irrigations of the bladder. On the twelfth day the catheter was removed, with no further urinary symptoms. He was discharged on the fifteenth postoperative day, weighing 135 pounds (61.4 Kg.).

On the twenty-fourth postoperative day his weight was 152 pounds (69.8 Kg.). He was eating well and was taking short walks. He complained of frequent "catching" pains in the left lumbar area during the day. One month postoperatively the tumor on his forehead was excised, and the microscopic diagnosis of this mass was lipoma.

High voltage roentgen ray therapy of the abdomen was administered from April 11 to April 22, 1947. A course of ten treatments was given. Five ports of entry were used. A 50 per cent skin unit dose was given over each, with 500 kilovolts and 7 mm. of copper.

On May 5, 1947, he weighed 169 pounds (76.7 Kg.), which was his weight before the operation. He complained of severe nausea, which began during the roentgen ray therapy and was associated with some cramplike pains in the upper part of his abdomen. On examination the abdomen was entirely normal; his blood pressure was 130 systolic and 80 diastolic. Treatment consisted of administration of a cerium oxalate–bismuth subnitrate mixture, tincture of belladonna and a low residue diet. With this regimen, he felt better for about three weeks. On May 28 the nausea and the cramps in the upper abdominal area again became severe. He was hospitalized on June 1. On his admission he appeared acutely ill and had a tinge of jaundice. After several hours he became comatose and the jaundice deepened.

Laboratory studies on the first day revealed bile and albumin (1 plus) in his urine. The blood nonprotein nitrogen level was 50 mg. per hundred cubic centimeters. The blood sugar content was 174 mg. per hundred cubic centimeters and the icterus index 46. The van den Bergh test gave a delayed direct reaction.

Treatment consisted of the intravenous administration of dextrose solution, blood transfusion and the use of vitamin K and oxygen. He did not respond to treatment and died three days later.

A necropsy was performed by Dr. Clarence I. Owen, who reported the following pertinent facts:

"The subject is a well developed, well nourished 52 year old white man weighing about 150 to 160 pounds (68 to 72.6 Kg.) and measuring about 170 cm. in length. The skin and sclera exhibit marked jaundice. There is about 10 cc. of bile-stained free peritoneal fluid. There are a few thin fibrous adhesions between the small bowel and abdominal incisional scars. There are numerous hard, nodular, lobulated, retroperitoneal masses on the left side varying from 4 to 5 cm. in diameter which form a mass 11 by 12 by 4 cm. in size. They extend from the level of the left renal vessel down over the lumbar and sacral regions of the spine and into the true pelvis, circumscribing the left iliac vessels. The masses are yellow to yellowish gray. On cut surface they are the same color. Many of them cut with a gritting sensation and are stony hard. Some of the masses are firm and elastic. The descending colon is adherent to the retroperitoneal masses but is not penetrated by it. The liver measures 22 by 17 by 7 cm. The surface is reddish gray and mottled. It is soft, spongy and friable for the most part, with some

firm areas. The capsule is of the usual thickness and strips with difficulty. The cut surface of the liver shows complete absence of the normal architecture. Some areas are dark red with a small amount of mottling and others are greenish and orange red with a "nutmeg" appearance. Most of the cut surface is extremely soft, spongy and friable and tears with extreme ease. The gallbladder is of normal size and consistency. The wall is about 1 mm. thick. It contains dark (almost black) thick bile. There are no stones in it. The mucosa

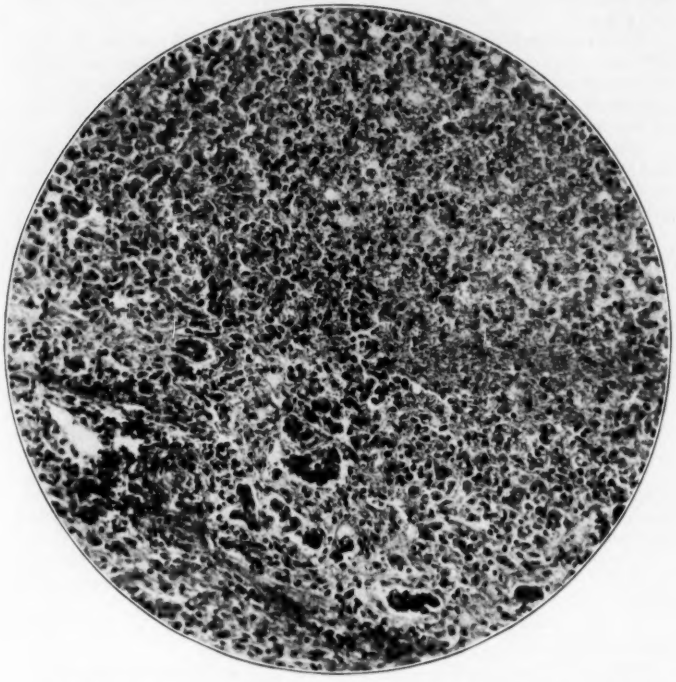

Fig. 7.—The normal architecture of the liver is lost. There is widespread necrosis of hepatic cells.

shows no gross pathologic changes. The cystic duct is normal in size and contains no stones. The common duct is normal in size and contains no stones or lesions. It is easily traced to the ampulla of Vater, and there is no obstruction in it. The hepatic ducts are traced with ease and are normal in size and contain no stones.

"Microscopic studies reveal that the liver exhibits complete loss of the normal architecture. The normal lobular arrangement is lost. The cells are necrotic (fig. 7). Associated with the necrosis there is extensive infiltration of inflammatory

cells and hemorrhage. The cells of the liver which do not exhibit either partial or complete necrosis contain large droplets of fat. The islands of Glisson are barely recognizable. Within them there is marked infiltration of inflammatory cells and edema. There is extensive new proliferation of bile.

"The retroperitoneal adipose tissue was thoroughly examined in numerous microscopic sections, and no evidence of malignancy is found. Within this tissue there is a considerable amount of fibrosis, small round cell infiltration and many large multinucleated giant cells of the foreign body type.

"All other organs show no serious histologic changes."

Pathologic Diagnosis.—The pathologic diagnosis was (1) acute necrotizing hepatitis (probably homologous serum jaundice produced by pooled blood plasma); (2) postoperative removal of retroperitoneal tumor (lipomyxosarcoma), with no evidence of recurrence, and (3) repair and foreign body reaction within retroperitoneal adipose tissue.

POSSIBLE HISTOGENESIS

The cause of retroperitoneal fatty tumors is as obscure as that of other tumors. More must be known of the character and the function of the fat cell before we can understand the origin, growth and behavior of these strange tumors. Wells [4] stated the belief that the fat cell is not a modified fibroblast existing for the sole purpose of storing fat but is a specialized fat-forming mesenchymal cell which on occasion can produce a wide variety of different and complex tissues. This might explain the frequency with which fatty tumors of the retroperitoneal space are associated with other tissues, particularly myxomatous.

It is believed by some that liposarcoma originates in preexisting lipoma. Schiller [5] cites three examples of lipomas which were excised and later recurred with sarcomatous change. The same process may have occurred in the case reported here in view of the fact that the tumor was associated with subcutaneous lipomatosis and previously removed inguinal lipomas. Haagensen and Krehbiel,[6] by injecting benzopyrine subcutaneously in guinea pigs, were able to produce tumors, 50 per cent of which were liposarcomas. These authors suggested that liposarcoma arises in adult fat cells as a result of long-standing chemical irritation and stimulation. Selman,[3d] on the other hand, removed a retroperitoneal tumor which was diagnosed as spindle cell sarcoma. On the occasion of two subsequent recurrences the diagnoses were myxosarcoma and lipomyxosarcoma respectively. Stout [1r] expressed the opinion that although some of the tumors may develop from preexisting lipoma, most are malignant from the beginning.

4. Wells, H. G.: Adipose Tissue: A Neglected Subject, J. A. M. A. **114**: 2177 (June 1) 1940; 2284 (June 8) 1940.

5. Schiller, H.: Lipomata in Sarcomatous Transformation, Surg. Gynec. & Obst. **27**:218, 1918.

6. Haagensen, D. C., and Krehbiel, O. F.: Liposarcoma Produced by 1:2 Benzopyrene, Am. J. Cancer **27**:474, 1936.

AGE INCIDENCE

The age was noted in 47 of the 53 cases of retroperitoneal fatty tumors reported from 1937 to 1947. The youngest patient was 2 years old and the oldest 86. The average age was 51.5. Approximately 70 per cent of all patients in this series were between the ages of 40 and 70. The average age in the cases of malignant tumor was 55; in the cases of benign tumor it was 48.

In a comparison of the various age groups in cases collected from 1937 to 1947 and in those in von Wahlendorf's [2] series, it is seen (table 2) that the greatest number are in the fifth and sixth decades in both series.

SEX DISTRIBUTION

Throughout the entire literature it is generally agreed that these tumors occur more frequently in females, in a ratio of about 2 to 1.

TABLE 2.—*Age Incidence in Cases Collected from 1937 to 1947 and in von Wahlendorf's Cases*

Age	No. of Cases	%	No. of Cases	%
0 to 20	3	6.3	10	7.8
20 to 40	8	17.0	40	31.0
40 to 60	23	49.0	72	55.8
Over 60	13	27.7	7	5.4
Total	47		129	

TABLE 3.—*Sex Incidence*

Sex	No. of Cases	Benign Tumors	Malignant Tumors
Male	17	5	12
Female	32	20	12
Total	49	25	24

The same ratio was found in the present collected cases. The sex was mentioned in 49 of the 53 cases. There were 32 females and 17 males. When the sex incidence in the cases of benign and malignant tumors was determined, it was found that of the 17 tumors in males 5 were benign and 12 malignant; of the 32 tumors in females, 20 were benign and 12 malignant. In other words, there was a ratio of 4 females to 1 male in the cases of benign tumor and a ratio of 1 to 1 in the cases of malignant tumor (table 3).

From these figures we should expect that a retroperitoneal fatty tumor in a male would have a two to one chance of being malignant and in the female a two to one chance of being benign. Why there is a greater disposition to malignancy in the male is difficult to explain. The sex ratio of the 6 cases involving children collected in the literature by Kretschmer [1h] was 1 to 1.

CLASSIFICATION AND TERMINOLOGY

Because of the varied admixtures of tissues found in these tumors, a number of confusing terms have arisen in the literature: lipoblastoma, pseudomyxomatodes, lipoma, malignant lipoma, lipoblastic myxoid sarcoma, liposarcoma and lipofibroblastic sarcoma. Stout [1r] looks on liposarcomas not as a group of separate and distinct types of tumor worthy of bearing separate names but as a single group capable of manifesting different degrees of differentiation which can be indicated by descriptive adjectives. With this conception in mind he subdivided liposarcomas in four groups: (1) well differentiated myxoid type; (2) poorly differentiated myxoid type; (3) round cell or adenoid type, and (4) mixed group (two or more elements of the preceding groups).

TABLE 4.—*Classification of Retroperitoneal Fatty Tumors*

	Collected Cases, 1937 to 1947 No. of Cases	To 1921 (von Wahlendorf) No. of Cases
Benign		
Lipoma	19	70
Fibrolipoma	4	31
Myxolipoma	3	16
Fibromyxolipoma	1	15
Fibromyolipoma	1	..
Total	28 (52.8%)	132 (86.2%)
Malignant		
Liposarcoma	7	3
Lipomyxosarcoma	13	13
Fibrolipomyxosarcoma	2	..
Fibroliposarcoma	2	5
Fibromyosarcoma	1	..
Total	25 (47.2%)	21 (13.8%)

The terminology used in table 4 depends largely on the diagnoses made in the case reports. It was found convenient to separate retroperitoneal fatty tumors into two main subgroups: benign and malignant. Under the benign group were placed all tumors, pure and mixed, not showing evidence of sarcomatous change and under the malignant group all tumors in which such change was present.

This classification must be accepted with reservations because benign retroperitoneal fatty tumors do not behave as do benign fatty tumors elsewhere in the body, inasmuch as they recur frequently and often sarcomatous changes are found in the recurrent growth. Boyd [7] stated:

> it is doubtful if a retroperitoneal lipoma merits such an innocent name. It does not consist only of fat; myxomatous and even sarcomatous areas may be discovered if a number of different parts of the growth be examined.

7. Boyd, W.: Surgical Pathology, Philadelphia, W. B. Saunders Company, 1942, p. 369.

Stout [1r] pointed out that often it is difficult to distinguish between myxolipoma, fibromyxolipoma and myxoliposarcoma microscopically. Some of the benign myxomatous tumors reported would probably have been included in Stout's first subgroup mentioned previously.

PATHOLOGIC PROCESS

One of the most characteristic features of these tumors is their frequent enormous size. This is easily understood because no resistance is offered these expanding growths until they have filled all available space. In some cases they have grown into the inguinal canals [8] and in others into the labium and buttock [9] and through the obturator foramen.[10] In the case reported here many lipomas were found in the inguinal canals three years previously. These may, however, have been independent tumors.

The weight of the tumor was mentioned in 35 of the 53 cases. The average weight was 16.3 pounds (7.4 Kg.). The largest tumor during this period was reported by McLaughlin and Sharpe,[1k] a lipomyxosarcoma weighing 56 pounds (25.5 Kg.) removed at autopsy. The largest tumor in the 1937 to 1947 series successfully removed was a liposarcoma weighing 38.5 pounds (17.5 Kg.) reported by Cattell and Warren [1c] in 1947. In 1935 Williams [3c] removed a lipomyxosarcoma weighing 51 pounds (23.2 Kg.) This is the largest primary fatty retroperitoneal tumor removed successfully to date. Delamater [11] in 1859 described a mammoth retroperitoneal fatty tumor which protruded outside of the left labium majus and buttock to form a mass 4 feet (121.9 cm.) in circumference, while the circumference of the abdomen was 7 feet 8 inches (233.6 cm.). Three years before her death the patient weighed 269 pounds (122 Kg.), of which 179 (81.2 Kg.) was estimated to be tumor. There is no record of an operation or an autopsy on this patient. The largest authentic tumor was a fibroliposarcoma reported by Hirsch and Wells [30] in 1920. Twenty-nine pounds (13.2 Kg.) of this tumor was removed surgically, and forty-eight hours later another 40 pounds (18.2 Kg.) was removed at autopsy, making a total of 69 pounds (31.4 Kg.)

Morgagni [12] in 1761 described the gross appearance of the first retroperitoneal fatty tumor, removed at a necropsy on a 60 year old woman. Virchow [13] in 1857 made the first microscopic study of one. The usual gross appearance of these tumors is not unlike that described in the case reported here. Some have reddish or reddish brown areas, usually indicative of hemorrhage or increased vascularity. Many are shiny and

8. Lundblad, cited by Frank.[1g]
9. Gough, A. J., cited by Donnelly.[1o]
10. Deupert, cited by Donnelly.[1o]
11. Delamater, cited by Stout.[1r]
12. Morgagni, J., cited by Masson and Horgan.[31]
13. Virchow, cited by McLaughlin and Sharpe.[1k]

mucoid in appearance. On cut section the tumor may be found either solid or containing cystic areas filled with mucoid or mucopurulent material. Areas of normal yellow fat are often interspersed among sarcomatous masses. Usually, however, even the largest remain solid throughout despite extensive areas of degeneration.

The histologic picture of the benign tumors in some cases is that of clusters of adult fat cells separated into irregular lobules by fine strands of connective tissue, the surface being covered by a thin connective tissue capsule. Frequently, however, the microscopic picture is extremely varied, giving rise to the great number of microscopic diagnoses seen in table 4. Myxomatous tissue is frequently present, and, as pointed out previously, benign tumors may be difficult to distinguish from malignant tumors of this type. The usual picture is an admixture of fatty, myxomatous and fibrous tissue.

In the more recently reported cases (1937 to 1947), 47.2 per cent of the tumors were sarcomas, whereas prior to 1921, in von Wahlendorf's series, sarcomatous change was recorded in only 13.8 per cent (table 4). Of Masson and Horgan's [3l] 12 tumors reported in 1921, 25 per cent were malignant. Pemberton and Whitlock [3b] in 1934 reported 33 per cent of 30 tumors to be sarcomas. This would indicate that present day pathologists are examining these tumors more thoroughly and are thereby recognizing sarcomatous changes more frequently.

Another prominent feature of the tumors is their tendency to recur. Benign lipomas often cannot be differentiated with subsequent recurrence, and with each recurrence the degree of malignancy usually becomes greater.[1k] There are cases recorded in which recurrent tumors have been removed five or six times. Distant metastasis is rare but has occurred in 2 cases in this collected series—to the liver in Moreland and McNamara's [1m] case and to the liver and lungs in Stout's case.[1r]

These tumors may arise from any part of the retroperitoneal space. The most common origin is the perirenal fat. Other sites are the renal capsule, the mesentery and the pararectal and retrorectal fat. When the tumors attain a large size, the original site is no longer determinable because they encroach on and adhere to any of the intra-abdominal organs. About 80 per cent of the tumors are abdominal and 20 per cent pelvic.[1k]

DIAGNOSIS

The clinical diagnosis of the tumors is usually difficult, particularly if they are small. As a rule symptoms are absent until the tumor has reached a large size, but even then the symptoms are not commensurate with the enormity of the growth. The average duration of symptoms before medical advice was sought was 33.22 months in the cases reported in this study. Some of the cases are discovered accidentally either during a routine examination or in the course of an abdominal operation.

Regan and others [19] accidentally discovered a retroperitoneal fibrolipoma while operating on a ventral postoperative hernia. The tumor weighed 16.5 pounds (7.5 Kg.). Usually, however, the patient notices a slowly progressive abdominal enlargement and eventually seeks medical advice. Associated with this may be vague digestive disturbances. Edema of the lower extremities may occur. As the tumor becomes larger the patient often loses weight and strength.

On examination a mass is usually palpable. If it presents into the pelvis it is often mistaken for an ovarian or uterine tumor, and in the lumbar region it may be mistaken for a renal tumor or a mesenteric or retroperitoneal cyst. When occurring as a large intra-abdominal mass it may be considered to be a pancreatic cyst, mesenteric cyst, abdominal carcinomatosis, splenomegaly, ascites, cirrhosis and pregnancy. At times a difference in surface temperature of the two lower extremities is suggestive of a retroperitoneal tumor producing pressure on the lumbar sympathetic nerves.

If a retroperitoneal tumor is considered in the differential diagnosis, a series of gastrointestinal roentgenograms and pyelographic studies will contribute valuable diagnostic information. Displacement of the small intestine, colon and stomach without an intrinsic lesion, as illustrated in figures 1 and 2 *A*, indicates a tumor outside of the gastrointestinal tract. Displacement of the kidney and the ureter, with possible distortion of the calices from pressure, usually indicates that the tumor is retroperitoneal. Pyelographic studies to determine renal function are also important in the event that a nephrectomy might be necessary at operation. Combining retroperitoneal air injections with roentgenologic studies has often been of value in localizing some of the smaller tumors.

To recognize preoperatively a retroperitoneal tumor as being lipomatous is almost too much to expect. A helpful clue would be an associated lipomatosis as found in the case reported herein. Windholz,[1w] in studying the radiolucency of the tumor, was able to make a correct preoperative diagnosis of retroperitoneal lipoma in the 3 cases he reported. The translucency of fat is due to its low absorption coefficient. With water considered as 1.000, the corresponding value of fat is estimated at 0.486. Thus increased radiolucency of areas previously occupied by intestinal loops, accentuated by their displacement, is, according to Windholz, suggestive of a retroperitoneal lipoma. Less radiolucency suggests additional connective tissue in addition to fat and may indicate malignant change.

TREATMENT

The only satisfactory treatment is surgical removal of the tumor whenever possible. Most of the tumors are operable because they are usually well encapsulated. Only 5 of the 53 tumors were found to be inoperable (table 5).

The earliest operation was reported in 1824 by Lizar,[14] who thought that he was dealing with an ovarian tumor, a mistake often repeated since. Encouraged by MacDowell's successful ovariotomy, he proceeded. He found the uterus and ovaries normal, but there was a flattened fatty tumor opposite the left sacroiliac synchondrosis, lying beneath the division of the common iliac arteries.

In 46 of the 53 cases reported the tumor was completely removed. Eleven, or 24 per cent, required nephrectomy. There has been a wide difference of opinion as to the number of such cases requiring nephrectomy—75 per cent according to Herman,[15] 50 per cent according to McLaughlin and Sharpe [1k] and 14 per cent according to Pemberton and McCaughan.[2a] Nephrectomy was necessary when separation of the tumor from the kidney was impossible, when the ureters or the renal vessel was injured or when hydronephrotic kidney was present.

The operation is not without considerable danger. Special care must be exercised to avoid injury to important blood vessels such as

TABLE 5.—*Treatment (Collected Series, 1937 to 1947)*

Treatment	No. of Cases
Total excision	34
Total excision with nephrectomy	11
Total excision with orchidectomy	1
Partial excision	2
Total operated on	48
Inoperable tumors	5
Postoperative roentgen ray therapy	6

the mesenteric arteries and veins, the abdominal aorta, the inferior vena cava and the renal vessels. Accidents to these structures have caused fatal hemorrhage and gangrene of the bowel. Intestinal resections have been necessary because of accidental ligation of the inferior mesenteric, middle colic or sigmoid arteries. Fatalities have been reported following perforation of the third portion of the duodenum. Injuries to the bladder, transverse colon and rectum have also been reported.

Even when the tumor is separated from the surrounding structures with ease, it may recur. This is probably due to the presence of satellite nodules in the region of the main tumor. Many of these smaller tumors exist in recesses not explored or are so small as to be undetected by the surgeon. As Seids and McGinnis [16] pointed out, islands of undif-

14. Lizar, cited by Masson and Horgan.[81]

15. Herman, L.: Practice of Urology, Philadelphia, W. B. Saunders Company, 1938, p. 265.

16. Seids, J. W., and McGinnis, R. S.: Malignant Tumors of the Fatty Tissue, Surg., Gynec. & Obst. **44**:232, 1927.

ferentiated tissue may be scattered about the site; these may be stimulated to active growth after removal of the primary tumor. It is therefore well to remove the main mass first, and, with more adequate exposure, to make a careful search for remaining tumor nodules hidden in folds and recesses.

In 1 of Cattell and Warren's [1e] cases the retroperitoneal tumor was continuous with one in the scrotum. Orchidectomy in addition to removal of the retroperitoneal tumor was necessary.

In 2 cases only partial excision was possible. In Stout's [1r] case a liposarcoma was partially removed, followed by high voltage roentgen ray therapy. The patient died fifteen months later with pulmonary and hepatic metastasis. In Fisher's case [17] one half of a retroperitoneal lipoma was excised. The specimen weighed 8 pounds (3.6 Kg.). The remainder slowly sloughed away, with purulent drainage for seventeen months.

The transperitoneal approach has been most frequently used in removing these tumors (84.6 per cent).[1g] Small tumors located in the vicinity of the kidney can be removed by the lumbar route. In some cases a lumbar approach was converted into a transperitoneal one in order to get more adequate exposures.

The use of high voltage roentgen ray therapy postoperatively in cases of malignant tumors has been of questionable value. Eleven authors in the recent literature commented on its value. Six of the authors believed that it was of some value postoperatively and also advised its use in inoperable cases. Three believed that it was of doubtful value, and two were of the opinion that it had no value at all. Stout [1r] stated that there has been some success with this form of therapy at Presbyterian Hospital and Memorial Hospital, and even though there have been failures and discouraging results, it should not be abandoned. Six patients in the present collected series received roentgen ray therapy postoperatively. Two were alive after eighteen months and two years respectively, and 4 died two, three, twelve and fifteen months, respectively, after operation.

RESULTS

Between 1937 and 1947, 48 patients in all were treated surgically. There were 4 hospital deaths, an operative mortality of 8.3 per cent. In the older literature the mortality was much higher. In von Wahlendorf's collective review [2] he stated that 25 per cent of the patients died during or at the conclusion of the operation. In Pemberton and McCaughan's [3a] series 8 of 42 patients (19 per cent) died in the hospital.

The 4 deaths in the hospital in the 1937-1947 series were due to mesenteric thrombosis,[1c] perforation of the duodenum,[1q] peritonitis [18] and

17. Fisher, A. O., cited in discussion on Nordland.[1x]
18. Hunt, C. J., cited in discussion on Nordland.[1x]

shock.[18] There was no report of fatal operative or postoperative hemorrhage in this collected series.

Of the 44 patients who left the hospital, 25 (14 benign and 11 malignant tumors) had follow-up records (table 6). Thirteen were living and well. Six of these, however, were observed for less than a year. Of the remaining 7, 4 who had benign tumors were well one and one-half, four, five and ten years, respectively, after surgical intervention. Three patients with malignant tumors were well one and one-half, two and eleven years, respectively, after operation. In 6 cases there were recurrences. In all these a diagnosis of benign neoplasm was made originally. Three of the recurrent tumors were considered to be sarcomatous. Six of the 25 patients died two, three, three, twelve, fifteen and eighteen months, respectively, after operation. These were all treated for malignant tumors originally. Since a total of 11 patients with malignant tumors were followed, more than 50 per cent of these patients died within eighteen months postoperatively. In Pemberton and McCaughan's

TABLE 6.—*Results (Collected Series, 1937 to 1947)*

	Number
Total number operated on	48
Deaths in hospital	4 (8.3%)
Total number followed	25
Living and well	13 (52%)
Recurrences	6 (24%)
Deaths	6 (24%)

series [3a] 57 per cent of all the patients died either at operation or within four years postoperatively.

PROGNOSIS

If left untreated, the tumors will usually increase in size and cause the death of the patient. Death in the cases of inoperable tumor in this study was considered to be due to the following complications found at autopsy: infiltration of the bladder, advanced hydronephrosis, compression atrophy of the kidney, perforation of the cecum, diffuse fetid peritonitis, compression atelectasis of the lungs, perforation of the duodenum and thrombosis of the iliac veins.

Operative mortality has been greatly reduced, no doubt because of improvement in preoperative and postoperative care, anesthesia and surgical technic. In cases of malignant fatty tumor, however, there was a high postoperative mortality, 55 per cent of the patients having died within eighteen months. A high percentage of the benign tumors have recurred. Six of 14 benign tumors, or 43 per cent, recurred in from seven weeks to five years. One half of these showed malignant change.

SUMMARY

A retroperitoneal lipomyxosarcoma weighing 29 pounds (13.2 Kg.) was successfully removed in a 52 year old male patient. Postoperatively, among other measures, 500 cc. of pooled blood plasma was given intravenously to combat shock. He made a satisfactory recovery, left the hospital on the fifteenth postoperative day and later improved rapidly and gained weight. High voltage roentgen ray therapy was administered six weeks postoperatively. During and after the therapy he complained of persistent nausea and vague abdominal distress. Three months postoperatively rapidly deepening jaundice developed, followed by coma and death. The most important finding at necropsy was extensive acute necrotizing hepatitis, probably homologous serum jaundice produced by the pooled blood plasma. There was no evidence of recurrence of the tumor.

Approximately 300 cases of retroperitoneal fatty tumors have been reported to date.

Fifty-three cases were collected from the literature from 1937 to 1947.

(*a*) Sarcomatous change was found in a much greater percentage of cases in this series than in the series in the older literature, i. e., 47 per cent as compared with 14 per cent in von Wahlendorf's study of 1921.

(*b*) The most frequent age was 40 to 60 years.

(*c*) The over-all sex ratio of females to males was approximately 2 : 1. In the cases of benign tumor it was 4 : 1, and in the cases of malignant tumor 1 : 1.

(*d*) The average weight of the tumor was 16.3 pounds (7.4 Kg.). The largest weighed 56 pounds (25.5 Kg.).

(*e*) Helpful diagnostic aids are associated lipomatosis, difference in the temperature of the lower limbs, roentgenologic evidence of displacement of viscera without intrinsic disease, radiolucency of the tumor and pyelographic evidence of displacement of the kidney and the ureter.

(*f*) Five tumors were inoperable. Of the 48 patients operated on, 4 died in the hospital, an operative mortality of 8.3 per cent. Of the remaining 44 who left the hospital recovered; 25 had follow-up records; 14 had benign tumors removed and 11 malignant tumors.

1. Thirteen were living and well. Six of these had been observed for less than one year.

2. Of the 14 benign tumors, 6 recurred, 3 of which had sarcomatous change.

3. Of the 11 patients who had malignant tumors, 6 died within eighteen months after surgical intervention. Two of the 5 who were living and 4 of the 6 who died had postoperative roentgen ray therapy.

TISSUE REACTIONS TO WAXES DERIVED FROM SPOOL COTTON

Possible Etiologic Relation to Suture Granulomas and Suture Extrusion

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AND
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SPOOL cotton is regarded as a satisfactory suture material by many surgeons. Its use was reported by Ginkovskiy [1] in 1936, and extensive investigations of its properties were made by Meade and Ochsner,[2] Meade and Long,[3] Localio and Hinton [4] and others.[5] Even workers reporting occasional difficulties with sutures of this material seem to prefer their continued employment.

Adverse reactions to cotton have been recorded, but in the main these seem to be less prevalent and less severe than those encountered with other materials.[6] Early experiences with cotton, as indeed with

From the laboratories of St. Peter's General Hospital.

1. Ginkovskiy, V. M.: Cotton Thread As Suture Material and Simple Method for Sterilization, Vestnik. khir. **44**:27, 1936.

2. (*a*) Meade, W. H., and Ochsner, A.: Spool Cotton As Suture Material, J. A. M. A. **113**:2230 (Dec. 11) 1939; (*b*) Relative Value of Catgut, Silk, Linen, and Cotton As Suture Materials, Surgery **7**:485, 1940.

3. Meade, W. H., and Long, C. H.: Use of Cotton As Suture Material, J. A. M. A. **117**:2140 (Dec. 20) 1941.

4. (*a*) Localio, S. A., and Hinton, J. W.: Choice and Use of Cotton for Suture Material, Surg., Gynec. & Obst. **72**:615, 1941. (*b*) Localio, S. A.; Casale, W., and Hinton, J. W.: Wound Healing: Experimental and Statistical Study, Internat. Abstr. Surg. **77**:457, 1943; (*c*) Wound Healing: Experimental and Statistical Study; Experimental Observations, Surg., Gynec. & Obst. **77**:243, 1943; (*d*) Wound Healing: Experimental and Statistical Study; Results, ibid. **77**:376, 1943; (*e*) Wound Healing: Experimental and Statistical Study; Bacteriology and Pathology in Relation to Suture Material, ibid. **77**:481, 1943.

5. (*a*) Large, O. P.: Comparison of Tissue Reactions from New Sutures, Am. J. Surg. **60**:415, 1943. (*b*) Dixon, J. L., and Ochsner, A.: Cotton Sutures and Ligatures, Bull. Tulane M. Fac. **3**:57, 1944. (*c*) D'Ingianni, V.: Cotton As Suture Material, South. M. J. **38**:786, 1945. (*d*) Kanne, W. P., and Smith, W. E.: Clinical Observations on Use of Cotton As Suture Material, Ohio State M. J. **41**:625, 1945.

6. Meade and Ochsner.[2b] Localio, Casale and Hinton,[4e] Large.[5]

other nonabsorbable sutures, have inculpated the use of unnecessarily coarse threads as the factor responsible for many of the reactions.[8b] Lack of experience with "cotton technic" and unfamiliarity with its exacting requirements accounted for others.[7] The use of cotton in cases complicated by bacterial infection or contamination has also, in the opinion of Derbyshire,[7] tended to increase the incidence of difficulties.

According to observations previously reported by others, suture extrusion, which is the principal difficulty arising from the use of cotton, is usually preceded by the appearance of a localized indolent induration, followed by a papule or vesicle and ultimate protrusion and discharge of a cotton knot. The entire process does not greatly inconvenience the patient. Persistently draining sinuses and proliferative reactions requiring surgical intervention are rare occurrences with cotton.[8]

Most of the recommended cotton threads are purchasable as "spool" or "sewing" cotton from the shelves of local handiwork shops on the supposition, confirmed generally in practice, that such threads are adequate surgically. Recently threads have been selected especially for surgical use, but here, too, regard was had mainly for the achievement of greater tensile strength rather than for chemical improvement of the product.

Cotton sewing thread is an evenly spun, plied yarn, hard twisted and smooth. It is fashioned from long staple cotton, usually of the Egyptian or sea island varieties. Between the stage of raw material and the finished product an elaborate processing intervenes, including selection and spinning of fibers, chemical bleaching, mercerizing and polishing. The thread may be boiled under pressure in caustic soda, bleached with hypochlorite solutions, "soured" in acid, boiled again with soap and caustic soda, rebleached with hypochlorite, soured again, soaped and hydroextracted in a final washing.[9] In the mercerizing process alkali is again employed. By now the cotton has been freed of easily soluble and saponifiable fatty materials and most other impurities. In the polishing or finishing process, a certain amount of waxy material of animal, vegetable or mineral origin may

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7. Derbyshire, R. C.: Complications Following Use of Cotton As Suture Material, Surg., Gynec. & Obst. **84**:31, 1947.

8. Orr, T. G.: Granulomas Caused by Surgical Silk and Cotton Sutures, Arch. Surg. **54**:37 (Jan.) 1947. Witter, J. A.: Unusual Proliferative Reactions to Suture Material, ibid. **56**:178 (Feb.) 1948. Meade and Ochsner.[2b]

9. Mervill, G. R.; Macormac, A. R., and Mauersberger, H. R.: The American Cotton Handbook, New York, The American Cotton Handbook Company, 1941.

be applied to produce a smooth nearly frictionless finish, in accordance with the manufacturer's formula. A product of high uniformity results.

Raw cotton contains 0.8 to 2.0 per cent of natural fats and waxes.[10] The analyses of Kettering and others[11] have shown that even after extensive processing cotton goods contain as much as 0.40 to 0.56 per cent of native waxes. These consist chiefly of higher alcohols and fatty acids (gossypol, montanyl and carnaubyl alcohols).[10] It occurred to us that these waxes, native as well as those added in processing, might not be entirely innocuous when introduced into living tissue and might possibly be dispensed with in the preparation of surgical suture cotton. In the case of waxlike substances of the paraffin series there are a number of reports of granulomas (paraffinomas) having been produced when such material was employed as an adjunct to plastic surgery.[12] Large[5a] has stated that the addition of wax or similar organic substances to increase the strength of silk sutures also increases the cellular inflammatory reaction in the tissues.

Information on certain tissue responses to wax derived from cotton was provided by Prausnitz,[13] who studied the effects of inhalation of cotton dust on the respiratory system. While of the opinion that waxes played little role in the respiratory disease under investigation, he nevertheless described the effects of an intradermal injection of 0.1 cc. of 1 per cent gossypol in human volunteers. Within three days a 5 mm. scarlet papule developed in the center of a 30 by 14 mm. area of redness. Within the next five days the papule grew to 10 mm., with fading of the surrounding redness. A "hard knob" remained for about five weeks.

METHODS

1. *Threads Tested.*—The following threads were tested: (*a*) "Kismet 00," white, mercerized, three cord thread, supplied by the American Thread Company; (*b*) "special thread," supplied by the Spool Cotton Company, ticket no. 70 and 30, and (*c*) thread supplied by Ethicon Suture Laboratories, size 000, white.

10. Hall, A. J.: Cotton Cellulose, New York, D. Van Nostrand Company, Inc., 1924.

11. Kettering, J. H.; Goldthwait, C. F., and Kraemer, R. M.: Solvent Extraction of Cotton Wax, Textile Research J. **16**:627, 1946.

12. (*a*) Wolf, G. D.: Paraffinoma of Nose: Case Report, Am. J. Surg. **55**: 153, 1942. (*b*) Cruickshank, A. H.: Paraffinoma of Peritoneum, Lancet **1**:4, 1941. (*c*) Cornbleet, T., and Popper, H. L.: Properties of Human Skin Revealed by Fluorescence Microscopy: Paraffinoma, Arch. Dermat. & Syph. **47**:637 (May) 1943.

13. Prausnitz, C.: Investigations on Respiratory Dust Disease in Operatives in the Cotton Industry Privy Council, M. Research Council, Special Report Series, No. 212, 1936.

2. *Method of Solvent Extraction:*—A modified Conrad procedure[14] was followed. The suture was loosely wound on a small glass tube and refluxed on an electric hot plate in ethyl alcohol for one hour, followed by similar treatment in chloroform for six hours. The extracts from each solvent were evaporated in tared small beakers and weighed. The resulting residue was pale yellowish to olive green, opaque and waxy in appearance and in odor. Practically all the alcoholic extract was soluble also in chloroform.

3. *Estimation of Tensile Strength:*—The Thwing-Albert pendulum type tensile strength tester[15] was used to determine the strength of straight and knotted threads. The suture diameter was measured with the Federal gager.[8][16]

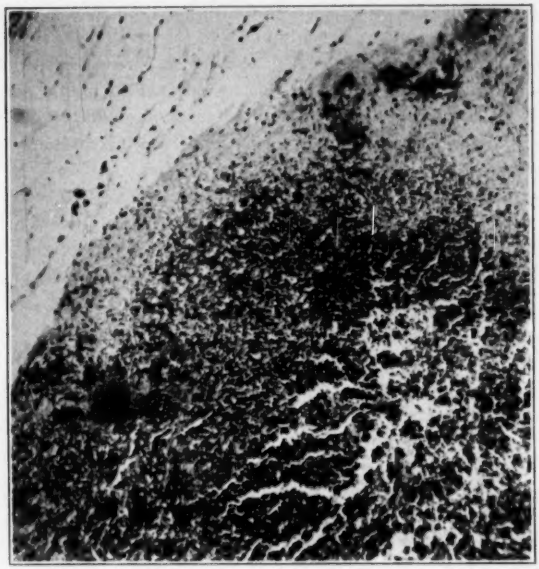

Fig. 1.—Reaction to implantation of cotton waxes (eleven days). Photomicrograph showing soft, abscess-like central portion and cellular exudate consisting mostly of polymorphonuclear leukocytes with some fibroblastic proliferation at the periphery.

4. *Introduction of Materials into Animals:*—(*a*) Rabbits were the only animals employed in these experiments. (*b*) The waxes were implanted intradermally

14. Conrad, C. M.: Determination of Wax in Cotton Fiber: Alcohol Extraction Method, Indust. & Engin. Chem. **16**:745, 1944.

15. Thwing-Albert Instrument Company, Philadelphia; courtesy of Dr. H. L. Davis, Ethicon Suture Laboratories, New Brunswick, N. J.

16. Federal Products Corporation, courtesy of Dr. H. L. Davis.

and subdermally, either surgically as single 2 to 4 mm. flakes or by hyperdermic syringe and needle in particulate form as an aqueous suspension. All materials were previously sterilized by autoclaving.

RESULTS

1. *Wax Content of Threads.*—The various specimens of processed spool cotton examined by us have yielded from 0.6 to about 4 per cent of waxy material as determined by ethyl alcohol–chloroform

Fig. 2.—Reaction to implanted cotton waxes (fourteen days). Photomicrograph showing evolution of "foam cell" granuloma.

extraction, the average being about 1 per cent. Two of the cottons had been submitted by commercial firms as especially designed for surgical sutures; these threads on analysis showed the two extremes of wax content mentioned.

2. *Tissue Reactions to Cotton Waxes.*—Introduction of waxy material derived from spool cotton is invariably productive of two consecutively occurring reactions regardless of whether the material is introduced as a single compact fragment or in the form of a particulate aqueous suspension. During the first five days following implantation

there appeared a slightly reddened, small, firm, indolent papule when the suspension was introduced intradermally or subdermally and a larger, firm, rounded, movable nodule (0.5 to 1.0 cm.) when a single piece of wax was deposited subcutaneously or between the muscle layers. Histologically the lesions presented an intense polymorphonuclear leukocyte response approaching abscess formation. In the case of the solid wax implant, the acute polymorphonuclear reaction persisted

Fig. 3.—Reaction to cotton waxes (twenty-five days). Photomicrograph showing granulomatous lesion in which wax-laden histiocytes predominate and including small foci of necrosis and leukocytic infiltration.

longer, namely eleven to twelve days (fig. 1). The acute reaction was strikingly similar to that reported after introduction of higher fatty acids into tissues.[17]

The early leukocytic phase is followed by the development of a granuloma. Grossly a localized nodule or area of induration is seen

17. Sabin, F. R.; Smithburn, K. C., and Thomas, R. M.: Cellular Reactions to Wax-Like Materials from Acid-Fast Bacteria, J. Exper. Med. **62**:751, 1935.

and felt. Microscopically an abundance of foamy or vacuolated histiocytes replace much of the leukocytic exudate, accompanied with moderate numbers of fibroblasts and a rare giant cell. Minute foci of necrotic tissue with necrobiotic polymorphonuclear leukocytes are scattered within this nodule, which is otherwise compact and discrete (figs. 2, 3 and 4). The lesion persists grossly for five weeks and longer, depending somewhat on the quantity of waxy substance introduced.

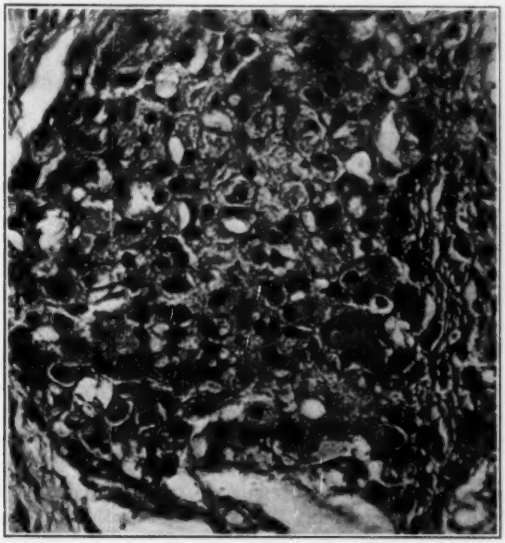

Fig. 4.—Higher magnification of figure 3 showing area of closely packed vacuolated histiocytes.

Results of Tension Tests

Thread	Wax Content, Percentage	Average Gage, Mils.	Average Breaking Point,* Lb.	
			Straight Strand	Knotted Strand
No. 70 (Spool Cotton Co.)	0.8	6.5	2.0	1.5
No. 70 (After extraction)	...	6.3	2.1	1.2
No. 30 (Spool Cotton Co.)	1.1	9.7	3.3	2.4
No. 30 (After extraction)	...	10.9	4.5	2.4
No. 000 (Ethicon Suture Co.)	4.2	10.3	4.5	2.8
No. 000 (After extraction)	...	10.3	4.9	2.6
No. 00 (American Thread Co.)	1.2	6.3	1.1	1.2
No. 00 (After extraction)	...	7.4	1.6	1.2

* The results listed apply to dry threads. Tests with wet strands, knotted and straight, before and after extraction were carried out with the Ethicon cotton, with results quantitatively comparable to those in the table.

3. *Tension Tests.*—Tests were carried out with several varieties of thread investigated, before and after solvent extraction, to determine whether "dewaxing" led to diminution of tensile strength. Both straight and knotted strands were tested. Sample results, illustrated in the table, indicate that some of the threads appeared actually to have been strengthened by treatment. This impression seemed best supported by tests made on straight rather than knotted strands. This observation was found, on subsequent search of the older literature, to have been made previously; Matthews [18] has stated that extraction of thread with solvents after spinning increases the strength but diminishes the "elongation" of the yarn.

COMMENT

The wide acceptance of ordinary sewing cotton as a surgical suture material is ample testimony to its general usefulness and relative freedom from difficulties. Wound complications following use of cotton sutures appear relatively few. However, continued reports of suture extrusion and suture granulomas point to the need for further study.

Our own observations seem to indicate that waxy substances, extractible by suitable solvents, are present in spool cotton in significant amounts and that these substances can produce acute inflammation and granuloma formation in living tissue. The clinical importance of these substances in the production of difficulties remains to be elucidated, since it is only the occasional patient who reacts adversely to cotton. The situation, however, may be analogous to that seen following the older practice of introducing paraffin wax under the skin as an adjunct to plastic surgery. Paraffinomas did not develop in all patients.[12a, b] Suture granulomas may similarly represent an idiosyncratic reaction to waxy substances introduced with the thread.

The removal of waxes by solvents does not seem to impair appreciably the gross physical appearance of cotton thread, nor does it have apparent deleterious effects on its tensile strength. The apparatus required for the solvent extraction of waxes from cotton suture material is simple and the operation easily carried out by any hospital laboratory.

SUMMARY

1. Analysis by extraction of several specimens of spool cotton showed that, in addition to cellulose, other materials, such as natural waxlike substances, are present in the threads and persist in significant amount after bleaching, washing and mercerizing processes. Additional waxy material is commonly added to the thread during its final finishing or polishing.

18. Matthews, J. M.: The Textile Fibers, ed. 4, New York, John Wiley & Sons, Inc., 1924, p. 469.

2. These substances may be responsible for some of the untoward effects reported following the use of cotton as sutures, chiefly the formation of suture granulomas and subsequent suture extrusion.

3. Experiments in rabbits showed that the waxy material extracted from spool cotton gives rise at once to an acute inflammatory reaction followed by the development of a "foam cell" granuloma which persists grossly for more than one month.

4. Solvent extraction of spool cotton was carried out and found to leave the tensile strength of the thread undiminished. Such a procedure is not difficult and affords a uniform product which is free of a significant group of tissue irritants.

A CLAMP FOR THE CONSTRUCTION OF VASCULAR ANASTOMOSES

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THE PROGRESS achieved in recent years in anesthesia, in preoperative and postoperative care and in surgical technic has allowed the surgeon to approach the heart and great vessels without fear of a prohibitive mortality rate. As a new field is opened, many instruments are developed to meet the unique and specific needs of the operative procedures.

Recently, work has been in progress on the construction of end to side and side to side anastomoses between the various great vessels. To facilitate the work, it was felt that a clamp should be designed that would satisfy the following requirements: 1. The instrument should be in two pieces, so that it can be applied and removed with the greatest ease; likewise, unless so constructed, it will be impossible to remove it after end to side anastomosis (as is the case with the Freeman clamp[1]). 2. The edges of the clamp should be so approximate that there can be no chance of its slipping or leaking and yet it will not injure the vessel wall. 3. Only a portion of the vessel used should be occluded. This not only allows a free flow of blood to take place during the operative procedure but also permits minimal mobilization of the vessel to be utilized. This is of particular importance when vessels of the portal system are being dealt with where hypertension exists and collateral circulation may be extensive. Use of the Potts clamp[2] in this situation would require complete mobilization of the vessel, which might well be impossible in the presence of the numerous collateral vessels. None of the existing clamps exactly fulfil all these requirements.

A clamp[3] has been designed, therefore, which, it is believed, will be of value in the construction of certain types of anastomosis (figs. 1 and 2). The clamp is in two parts, which allows easy application and

From the Department of Surgery, University of Illinois College of Medicine.

1. Freeman, S.: Studies on Eck Fistulae in Dogs, Surg. Gynec. & Obst. **87:** 735, 1948.

2. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of the Aorta to a Pulmonary Artery, J. A. M. A. **132:**627 (Nov. 16) 1946.

3. Made by Bruno Richter and Company, Glen Ellyn, Ill.

removal. The fine teeth which Potts [4] first described in the construction of his ductus clamp are utilized here. We have noted no instance of damage to the intima of the vessels after the application of these clamps. On the other hand, there is a firm grasp of the tissues within the instrument which precludes its slipping during the construction of the anastomosis. It is so designed that it is applied only to a segment of the vessel, thus never completely occluding the flow of blood and permitting minimal mobilization of the vessels involved (fig. 3).

Fig. 1.—The arms of the instrument are manipulated by means of the screw placed at the top of the handle. Note the fine teeth along the occluding surface of the arms which grasp firmly but do not injure the vessel segment.

For side to side anastomoses mirror image clamps are used. The handles thus are out of the field and lend mutual support for

4. Potts, W. J.: A New Clamp for Surgical Division of the Patent Ductus Arteriosus, Quart. Bull., Northwestern Univ. M. School **22**:321, 1948. Potts, W. J.: Surgical Treatment of Patent Ductus Arteriosus, Surg., Gynec. & Obst. **88**:571, 1949.

stability at the suture line. The right angle between the handle and the jaws of the instrument makes it possible to apply it in a narrow space.

The clamp has been used in the construction of portacaval anastomoses in a series of dogs. The suture technic was employed and 5-0 Deknatel silk on a no. 9 minimal trauma needle was used. The instrument was found to function satisfactorily and to meet the requirements established. The clamp was also used clinically [5] in the

Fig. 2.—The instrument can be separated into two component parts for application and removal.

construction of a splenorenal shunt, in which it was applied to the renal vein. Since only a portion of the vein was occluded, it was possible to perform the operation without mobilizing or occluding the renal artery. The possibility of use in the Potts operation, in which the instrument could be applied both to the pulmonary artery (thus alleviating the necessity of temporary ligation of the various segmental

5. By Dr. Ormand C. Julian.

branches) and to the aorta, without dividing the intercostal arteries, has been investigated experimentally in dogs, and in our opinion it facilitates the operative procedure. Work is now in progress utilizing the clamps in the construction of anastomoses employing arterial grafts. The results of this investigation will be published subsequently.

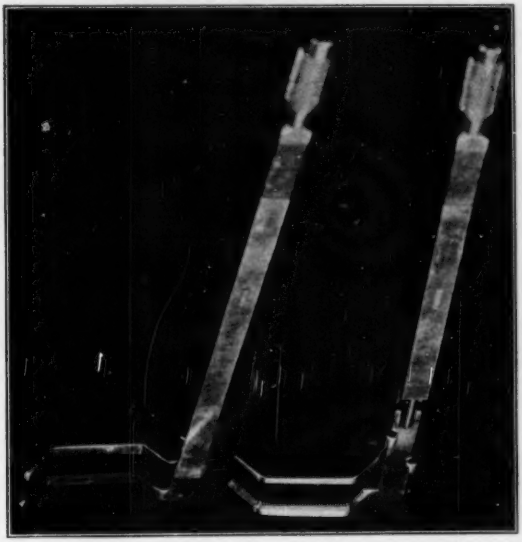

Fig. 3.—The angulation of the arms of the clamp allows adequate space for the construction of the anastomosis.

SUMMARY

A new clamp, which allows isolation of a segment of two adjacent vessels and construction of an anastomosis between them without mobilization or temporary ligation of either, is described. Optimum use of such an instrument is obtained by the construction of two clamps, one a mirror image of the other.

FULL THICKNESS PEDICLE FLAP GRAFT FROM THE AMPUTATED ARM FOR LARGE SKIN DEFECTS FOLLOWING INTER-SCAPULOTHORACIC AMPUTATION

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IN THE performance of interscapulothoracic amputation of the upper extremity, the sacrifice of a large amount of skin is at times necessary. These large defects pose a problem with regard to the matter of a satisfactory closure. Most surgeons have utilized the split thickness skin graft. Although such grafts are predominately successful, certain disadvantages of this type of closure are obvious. These disadvantages revolve about the following considerations: (1) the placement of a split thickness skin graft on an area which cannot be sufficiently immobilized, (2) the time consumed in preparing the skin, draping, cutting the skin grafts from the donor site and suturing them into the recipient site, (3) the addition of the granulating area of the donor site and (4) the resulting thinness of the thoracic wall covered in this fashion. An injury in this area readily may result in a communication with the thoracic cavity.

A recent experience with the use of a full thickness pedicle flap obtained from the superior surface of the extremity to be amputated provided an excellent solution for the patient involved.

REPORT OF A CASE

One month previous to his admission to the hospital on April 13, 1948, the patient, a 57 year old man, noted a "bump" in the left posterior axillary area. Two weeks later a "rheumatic-like" pain was experienced in this area. The pain gradually became worse.

The physical examination revealed nothing remarkable except for a firm, fairly smooth, spindle-shaped mass within the muscle bundle of the posterior axillary muscle group, attached laterally to the inferior angle of the left scapula. It measured 8.8 by 13.8 cm. and was movable.

A roentgenogram of the chest did not show evidence of any metastatic involvement.

All laboratory examinations revealed normal values for the hemoglobin content, white blood cell count, blood urea nitrogen, sedimentation rate and urine. Negative reactions to Wassermann and Kahn tests were obtained.

From the Department of Surgery, University of Minnesota, Minneapolis, Minn., and The Surgical Service, Ancker Hospital, St. Paul, Minn.

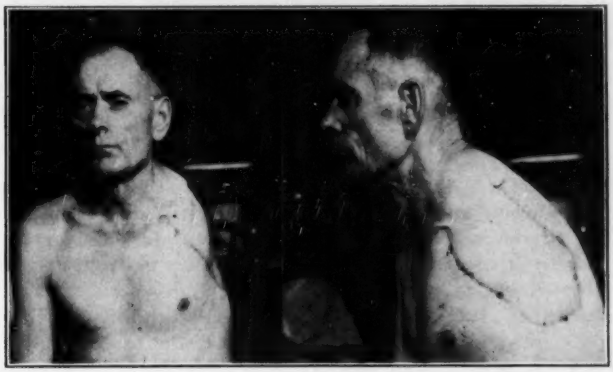
The clinical impression was that the mass was a sarcoma, possibly a rhabdomyosarcoma.

Operation.—Operation was performed on April 20, 1948, under anesthesia, produced by thiopental sodium and curare supplemented by the intratrachael administration of nitrous oxide. The tumor mass, which appeared to be incorporated in the latissimus dorsi, was excised locally with the lower quarter of the scapula, and a modified axillary dissection carried out. The tumor was entered into in one area.

The patient's convalescence was uneventful.

Pathologic Report.—The tumor was reported to be a rhabdomyosarcoma by Dr. John F. Noble.

Follow-Up Study.—On June 12, 1948, the patient returned to the outpatient department complaining of a dull aching sensation in the operative site. There was evidence of a recurrence under the arm and in the area of the previous



Anterior and lateral views of the patient one month postoperatively. The pedicle flap measured 10 cm. at its base (12.5 cm. in its greatest transverse diameter) and 22.5 cm. in length. The original defect measured 45 cm. transversely and 49.5 cm. in length.

excision. Lymphedema of the left upper extremity was present. A roentgenogram of the chest revealed a suspicious area of increased density in the left base which "probably represents a nipple shadow although a metastasis cannot be ruled out on this examination." In view of the discomfort in the operative area and the presence of recurrence with threatening ulceration, an interscapulothoracic amputation was advised. It was felt that if the thoracic lesion was, in truth, the result of metastasis, the amputation should be performed with the possibility of an excision of the intrapulmonary lesion at some later date.

The patient was readmitted to the hospital on June 21, 1948. On June 23, with the patient under thiopental sodium and curare anesthesia supplemented by the intratracheal administration of nitrous oxide, a left interscapulothoracic amputation was performed.

It was apparent that a large amount of the skin surface of necessity would be sacrificed. In resolving this problem, the possibility of obtaining split thickness grafts from the arm to be amputated was considered. However, instead it was

decided to fashion a pedicled flap graft of skin from the superior surface of the arm. The incision was begun immediately below and almost parallel with the clavicle. Through it a portion of the clavicle was excised and the division and ligation of the major vessels and the brachial plexus was completed. The incision then was carried down over the anterior border of the arm to within approximately 5 cm. of the elbow and transversely across the arm and up the posterior border, fanning out superiorly over the posterior thoracic wall so that a fairly wide base was allowed for the pedicle. This flap of skin and subcutaneous fat then was dissected off the fascia of the arm. A wide excision of the skin involved with recurrence was carried out when the extremity was amputated. The defect measured 45 cm. transversely and 49.5 cm. from the top to the bottom. The edges of the skin anteriorly, inferiorly and posteriorly were undercut in order to establish greater mobility. The pedicle flap graft was inserted into the defect and sutured to the skin edges about the periphery without undue tension. Approximately 8 cm. of the distal portion of the pedicle flap was in excess of the need and was sacrificed. A single split Penrose drain was inserted through the most dependent area of the closure. The stitches were removed on the seventh and tenth days. The wound was healed completely.

One month postoperatively the pedicle flap graft measured 10 cm. at its base (12.5 cm. in its greatest transverse diameter) and 22.5 cm. in length (see figure).

COMMENT

The use of a full thickness graft obtained from the superior surface of the extremity to be amputated undoubtedly will fill a definite need of the surgeon in selected cases. This procedure will find its greatest application in cases in which, because of the nature of the lesion or the involvement of skin by tumor, a large cutaneous defect will result from the operation. It can be used only in cases in which the superior skin of the extremity is uninvolved and somewhat distant to the primary or recurrent growth. It is my opinion that the procedure will be applicable to a large percentage of patients subjected to radical amputation of the upper extremity.

The merits of the procedure relate themselves to the following advantages: (1) the simplicity of obtaining the skin, (2) the use of a full thickness skin graft, which results in a protective covering and a 100 per cent "take," (3) the saving of valuable time which previously has been utilized in preparing the skin and draping, cutting and suturing split thickness skin grafts and (4) the avoidance of the granulating surface of a donor site.

SUMMARY

A simple procedure has been described which is applicable to patients subjected to interscapulothoracic amputation in whom a large surface area of skin must be sacrificed. By the use of this method, one can avoid, even in extensive defects, the necessity of using split thickness grafts. The multiple advantages of this procedure and a representative case have been discussed.

REVIEW OF UROLOGIC SURGERY

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(Continued from Page 202)

PENIS

Peyronie's Disease.—Fricke and Varney [34] report on Peyronie's disease and its treatment with radium. They state that fibrous plaques of the penis do not disturb vital function and that the condition is not serious; however, the disease tends to cause severe mental distress and every effort should be made to cure the condition. The patients are usually middle aged. It appears to be a self-limiting process. Although formerly this was considered an extremely rare disease, many more cases are being reported in recent years than formerly. The etiology is not known. On microscopic examination excised fibrous plaques resemble keloids elsewhere in the body. Hence, trauma due to previous infections, passage of sounds or some other factor may well be the cause. Although present methods of treatment are unsatisfactory, radium therapy given by the technic employed in treating keloids appears to be worth while. More than half the patients treated should receive definite benefit. Radium treatment of 141 patients in a period of six years is described; 44.6 per cent of those traced were not benefited,

34. Fricke, R. E., and Varney, J. H.: Peyronie's Disease and Its Treatment with Radium, J. Urol. **59**:627 (April) 1948.

but the remainder were helped. The age of the patient, duration of symptoms before treatment and number of treatments given did not seem to be factors definitely influencing the result.

Hypospadias.—Brendler [35] describes a simple method of repair for hypospadias which allows for extension of the channel to the distal limit of the glans penis. The essential feature of this method is the establishment of a trough on the ventral aspect of the gland during the first stage of operation for release of chordee. As healing takes place, this trough becomes completely epithelized and thus provides additional skin for the construction of a channel to the tip of the glans penis. The second stage of operation is carried out in the manner of the Thiersch-Duplay technic. The results of this method have proved most satisfactory. Five of 6 patients who underwent the complete procedure now have a glandular urethra.

Howard [36] studied an unselected group of 14 males having hypospadias, with the use of the endoscope and roentgenograms, for remnants of the caudal ends of the müllerian ducts. In penile hypospadias, the utricle is normal. In penoscrotal and perineal hypospadias, the prostatic utricle is markedly enlarged and may communicate with a well developed uterus. The findings are presented as evidence for an intersexual type of development rather than a purely local developmental error as the cause of these anomalies. Other causes of utricular dilatation or enlargement are discussed.

Smith and Blackfield [37] use Blair's first stage correction of the chordee without change. The correction of the chordee should be performed when the boy is about 18 months of age so that the corpora cavernosa will develop normally. Wide exposure of the corpora cavernosa allows thorough resection of fibrous tissue. Fibrosis along the ventrolateral borders of the corpora as well as in the intercavernous septum is a constant finding and yet it has been stressed by only a few authors. Identification of the fibrous bands is facilitated by subjecting the penis to extreme dorsiflexion over the fingers of the left hand and then scratching across the corpora with the tip of the knife. The increased area of the ventrum is covered by preputial flaps so that the urethra, to be made at the second operation, will consist entirely of skin which is hairless and elastic. Skin flaps are handled with hooks to minimize trauma. Bleeding vessels are tied with 5-0 plain surgical gut, while all skin sutures are of interrupted fine cotton. The second stage should not

35. Brendler, H.: A New Method for the Construction of a Glandular Urethra in Hypospadias Repair, J. Urol. **59**:1164 (June) 1948.

36. Howard, F. S.: Hypospadias with Enlargement of the Prostatic Utricle, Surg., Gynec. & Obst. **86**:307 (March) 1948.

37. Smith, D. R., and Blackfield, H. M.: A Modification of the Blair Procedure for the Repair of Hypospadias, J. Urol. **59**:404 (March) 1948.

be undertaken until three months after the first operation. A urethra of generous caliber can be made because skin for replacement is to come from the scrotum. The width of the penile skin flap to be used to form the new urethra need not be limited since the denuded area can easily be covered by scrotal skin. The cosmetic result afforded might be criticized because of the transplanted scrotal skin, which is not only hair bearing but is thicker than penile integument. If, after adulthood has been reached, a patient finds the appearance of his transplanted scrotal skin to be unsatisfactory, it would be feasible to replace it with a full thickness graft from some non-hair-bearing area, with normal erections possible. In the past eight years the authors' modification of the Blair technic has been applied to 20 patients, in 14 of whom it has been carried through to completion. Of the latter, 7 had no complications. In each of the remaining 7 a urinary fistula developed at the proximal end of the new urethra, but 5 patients enjoyed successful closure in conjunction with the third stage procedures. Only 2 of the 14 patients, then, required a fourth operation for completion of their repairs.

Hand [38] reports that a modified three stage operation, using a foreskin graft, has been suggested for the repair of hypospadias. This operation makes available adequate tissue for covering denuded surfaces and urethroplasty, permits inversion of the suture lines without tension and minimizes the formation of postoperative fistulas. Emphasis was placed on the following points: (1) a dry operative field; (2) spacing of lateral incisions to allow a flap wide enough for construction of a well calibrated urethra; (3) allowance for a wide urethral base to insure an adequate supply of blood; (4) meticulous approximation of inverted skin edges without tension, with the use of interrupted mattress sutures; (5) staggering of the suture lines by rotating the inner tube to one side and anchoring it under the lateral skin edge; (6) calibration of the healed urethral channel before the third stage repair; (7) destruction of all hair follicles near the proximal urethra prior to the third stage repair, and (8) support of the third stage suture line by means of a piece of rubber catheter on either side of the incision.

A case of penoscrotal hypospadias is reported. The patient was 13 years of age when the first stage of the operation was carried out. The opinion is presented that the type of urethroplasty contemplated is more important than the age of the child in determining when to undertake the operation for straightening the penis. Diversion of the urinary stream is not deemed necessary when a three stage operation is done.

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38. Hand, J. R.: Three Stage Repair for Penoscrotal Hypospadias: Report of a Case, J. Urol. **59**:414 (March) 1948.

URETHRA

Stricture.—Beard and Goodyear [39] report on their study of urethral stricture. The disease is caused by gonorrhea principally, but it is also the result of trauma, periurethral inflammation and urinary extravasation. Strictures which result from gonorrheal inflammation require an average of twenty-one and a half years to produce symptoms, while those resulting from trauma or periurethral inflammation are well formed within a few months. The incidence is much higher in the Negro race because of the prevalence of gonorrhea and its complications. Approximately 57 per cent of strictures occur when the patient is between the ages of 30 and 50 years; only 10 per cent occur at an age of less than 30 years. Stricture results from localized thrombophlebitis of the corpus spongiosum by direct extension of gonorrhea, by extravasation of antiseptic solution introduced by retrograde injection, by trauma to the corpus spongiosum penis or by generalized thrombophlebitis resulting from periurethral abscess or phlegmon. Pathologically, a stricture is composed of fibrous tissue which involves the outer coats of the urethra, the corpus spongiosum penis and Buck's fascia. The scarring which takes place in the latter structures which surround the urethra is the fundamental factor in strictures. Eleven per cent of strictures are multiple. The disease occurs in that part of the urethra surrounded by the corpus spongiosum. It most frequently occurs in the bulbous portion but is found in all parts except the proximal 1 cm. of the anterior urethra. Multiplicity, length and caliber can be accurately measured by urethrograms. The urologic adage that prostatic hyperplasia does not occur in combination with stricture is not substantiated.

BLADDER

Neoplasm.—The general review of papillomatosis of the bladder by Michon and Delinotte [40] is based on a study of the detailed reports of 90 cases, including 31 cases observed by the authors, and on replies to questionnaires sent to numerous outstanding French urologists, 18 of whom took part in the discussion. Michon and Delinotte regard single and multiple papillomatosis of the bladder as a single entity of potential malignancy. The pathogenesis of the disease is obscure, but it is believed most probably to be caused by a virus. The usual age of the patients has been reported as being from 30 to 50 years, but recently many cases were reported of patients beyond the age of 50 years, some being more than 70 years of age. Chronic irritation, either

39. Beard, D. E., and Goodyear, W. E.: Urethral Stricture: A Pathological Study, J. Urol. **59**:619 (April) 1948.

40. Michon, L., and Delinotte: La papillomatose vésicale, Rapp. et inform. A. franç. d'urol. **41**:1 (Oct. 10) 1947.

by exposure to certain chemicals or by bacteria and toxins in the urine at the ureteral orifice, is definitely a contributing factor. Hematuria is the chief symptom. Necrosis of papillomas may lead to cystitis or their calcareous incrustation to the formation of small calculi. Diagnosis is made by means of cystograms and stereocystograms. Pathologically the growths bear a striking resemblance to rectal polyposis. True recurrences are usually late; the earlier recurrences, known as pseudorecurrences, are usually due to incomplete removal or development later of initially invisible lesions. Recurrence in situ is considered a sign of malignancy, as is also the presence of an edematous collarette about the base of the tumor. Recurrence is reported in about 10 to 35 per cent of cases and is more frequent after endoscopic electrocoagulation than after incision of the bladder.

Recurrence is likewise more frequent in a case of diffuse or numerous papillomas than in a case of large single papilloma. Histologically, the polyps may be fibroepitheliomas or papillary epitheliomas, the latter being malignant. After destruction of one papilloma, remaining ones may disappear, as in the case of verrucae. Since pyeloureteral papillomatosis is as rare as vesical papillomatosis is common, routine examination of the ureters and kidney can be dispensed with except in the presence of hematuria at the ureteral orifice or a papilloma exteriorizing from the ureteral orifice only on ejaculation. Combined vesical and pyeloureteral papillomatosis may be an indication for nephroureterectomy in addition to the usual vesical treatment. For papilloma of the calices, total ureterectomy with removal of the vesical cornua is indicated. Ureteral papillomatosis after total cystectomy indicates diffuse involvement of the entire urinary tract. In contradistinction to endoscopic methods, vesical incision affords a better exposure as well as opportunity for extemporaneous histologic examination. If the latter reveals papillary epithelioma, surgical removal should be followed by implantation of radium needles. Unless they are numerous, fibroepitheliomas can be removed surgically. Small polyps can be treated by fulguration, and endoscopic therapy is always justified as an initial attempt. However, all patients must return for periodic examination for recurrence. Wide plaques can be excised widely with the electric bistoury, since the vesical mucosa has a marked tendency toward regeneration. After these interventions the bladder is only partially closed over a Marion tube. Partial cystectomy is indicated for infiltrating growths. Total cystectomy in two stages is recommended only for cases of diffuse papillomatosis and requires preliminary derivation of the urine.

Other methods of treatment less frequently used are described, including roentgen ray, contact radiotherapy and radium therapy, telecurietherapy, as well as treatments with various drugs such as irriga-

tions with silver nitrate, 95 per cent alcohol, alcohol and 50 per cent glycerin and 10 cc. of 20 per cent collargol® (a colloidal silver preparation).

Spinal, epidural and rectal anesthesia are recommended. Chevassu recommends nitrogen protoxide autoanalgesia. According to Jeanbrau, atypical cells in the urine present a contraindication to fulguration owing to the danger of neoplastic cystitis. Aspiration of the polyp prior to diathermic destruction has been found of aid. Endoscopic electrocoagulation is carried out in a single sitting with the patient under anesthesia. Luys recommends the direct vision cystoscope. If not too numerous, and if the area is accessible, recurrences may be treated endoscopically. The use of the urethroscope or resectoscope may facilitate treatment of papilloma about the neck of the bladder or posterior urethra. Almost immediate hemostasis is effected by radium or roentgen therapy. In cases of diffuse papillomatosis, electrocoagulation through a vesical incision may be attempted as an initial measure. Radiotherapy may cause cystitis, endoscopic treatment has been known to cause perforation of the bladder and vesical incision carries the risk of phlebitis and embolism. Total cystectomy is the treatment of choice for papillomatosis of the bladder which is widespread or which has failed to respond to endoscopic treatments. Radical treatment should not be delayed too long, since the disease may spread to other portions of the urinary tract. The prognosis of total cystectomy has been improved by the use of sulfonamide compounds and penicillin. Since partial cystectomy rarely yields cures, it might be best to follow the trend apparent in America, namely, the performance of total cystectomy while the patient's condition still permits. A radiologist should be present at the operation. If roentgen therapy is used, colchicine may be instilled to reenforce the effect of the rays. Gouverneur reports his experiences in 212 cases and Viollet reports on 70 cases. The latter recommends a loop to guillotine the polyps and likewise a bent, double Pezzer tube without a cap. Heitz-Boyer considers vesical papillomatosis to be of inflammatory and probably infectious origin. He dismisses potential malignancy as a metaphysical hypothesis and emphasizes the importance of the practical benignity of the disease. He warns against the combination of radiotherapy with high frequency roentgen therapy, since coagulated areas will undergo necrosis under the influence of the rays. He states that high frequency roentgen therapy will yield cure in the great majority of cases, and discusses in detail the best route, instrumentation and current. Incision is indicated according to Michon whenever the site of implantation is invisible, when papillomas are located on the anterior surface of the apex of the bladder and in the pericervical region.

Two arguments offered by Couvelaire and Pellot [41] in favor of partial cystectomy are that (1) it permits removal of the corresponding lymphatic region and (2) it leaves intact a small portion of the bladder, thus solving the problem of urinary diversion. However, trigonal cystectomy seems to have no advocates. Häberlin reported a case in which death resulted. Only a small portion of the bladder needs to be conserved to afford adequate capacity after ureterocystoneostomy. Recently Couvelaire and Pellot discovered that trigonal cystectomy is not difficult and that it yields excellent immediate results.

The patient was a man, 52 years of age, who had suffered from increasing dysuria for three years with pollakiuria and hematuria, the latter having recently become total and persisting for two days. Cystoscopy revealed an enormous red, irregular, infiltrating tumor which involved the entire trigone and vesical neck. The left ureteral orifice was invisible, and the one on the right was located with difficulty because it was partially masked by the tumor. Urograms revealed good renal secretion on both sides. After vesical extraperitonealization the external iliac lymph glands were inspected and appeared intact. The bladder was then incised. The entire trigone was involved in a red, sessile fleshy mass invading the left ureteral orifice and extending to within 1 mm. of the right ureteral orifice. In this case total cystectomy would seem to be indicated.

However, the complete integrity of the dome of the bladder and the possibility of conserving a flexible wing insuring its vascularization suggested that in this case trigonal cystectomy might solve the problem. The base of the prostate was resected, and the dome of the bladder separated from the trigone by a vesical incision, followed by section of the ureters. The entire trigone and the seminal vesicles were removed and the two ureters reimplanted in the dome of the bladder, which was closed over a Pezzer tube. The neobladder was then fixed to the oozing base of the prostate, the cellular spaces were drained and a sulfonamide drug applied locally. Eighteen days later urograms revealed good renal function, with slight atony of the excretory tract. The second stage was done one month after the first. Puncture of the bladder yielded escape of a small amount of turbid retained urine. The bladder was closed. Seven days later the urethral catheter was removed, micturition was painless and the patient was perfectly continent. The capacity of the bladder was 120 cc. Urograms showed that secretion was equal on both sides, with slight bilateral pyelic stasis. Cystograms showed slight vesicoureteral reflux on the right side. The silhouette of the bladder was like a mushroom with a thick stalk and

41. Couvelaire, R., and Pellot, C.: Sur les variantes de la cystectomie pour tumeur et singulièrement sur une technique de cystectomie trigonale, Rapp. et inform. A. franç. d'urol. **41**:323 and 331 (Oct. 7) 1947.

small head. Histologic examination revealed a pavement epithelium infiltrating the muscle. The segment of the prostate showed numerous glands, all with normal covering.

The psychologic effect of the operation on the patient is wonderful. Micturition is easy, painless and surprisingly infrequent, considering the small portion of the bladder left in situ. It is emphasized that the vesical muscle has a marked tendency to regenerate. The authors attribute the perfect control of micturition to integrity of the striate sphincter. It is impossible to guarantee that the vesical dome will not subsequently undergo ischemic necrosis. Further research on the vascularization of the dome of the bladder and permeability of the umbilical artery should afford new information in this field.

Gouverneur and Dufour [42] state that in the performance of wide cystostomy, which is frequently employed for partial cystectomy, often the neoplastic area is entered, and thus there is the risk of operative dissemination. The tumor is then widely excised, but the perivesical tissue, lymphatic vessels and glands are left in situ. No histologic control is made during the operation to insure that all traces of neoplastic process have been removed. The fact that the excision is carried into apparently normal tissues means nothing. The operation is concluded by suture of the vesical tissue, with or without reimplantation of the ureters. The mortality rate of partial cystectomy ranges from 11 to 55 per cent, the average being 25 per cent. Recurrence is reported in from 35 to 90 per cent, most recent figures being 50 to 56 per cent. The question is brought up of why partial cystectomy should continue to be used when partial operations on the rectum and uterus have long since been abandoned.

The main objections to total cystectomy are (1) serious operative prognosis, (2) the resulting infirmity, (3) inadequacy of exeresis and (4) the anatomic difficulties in execution. The operative mortality rate of total cystectomy is considerably lower in two stage than in one stage operations. Gouverneur and Dufour prefer intestinal implantation of the ureters as a preliminary operation, employing Coffey's technic no. 1. If only one ureter is available for transplantation, the approach is through a lateral incision via the subperitoneal route.

Intestinal diversion of the urine is greatly aided by preoperative and postoperative measures, such as prolonged evacuation of the intestines, a nutritious, low residue diet and disinfection of the intestinal contents with sulfaguanidine or, better still, succinylsulfathiazole. Penicillin also is a valuable adjunct. For three days after anastomosis, Millin recommends daily intravenous infusion of 1 liter of isotonic sulfate serum, 1 liter of isotonic saline solution and 1 liter of dextrose serum.

42. Gouverneur, R., and Dufour, A.: La cystectomie totale dans le cancer de la vessie, Rapp. et inform. A. franç. d'urol. **41**:318 (Oct. 7) 1947.

The mortality rate of the subsequent cystectomy can be reduced by such measures. As regards the residual infirmity, patients unanimously prefer the intestinal to the cutaneous implantation of the ureters. If the anastomosis is performed on an intact renoureteral apparatus, renal function is good, thanks to preliminary chemotherapy.

Total cystectomy includes removal of the perivesical fatty tissues, including numerous lymphatic vessels and juxtavesical glands. Operative dissemination is responsible for most recurrences. Distant metastasis is rare. The hypogastric lymphatic vessels left in situ form a focus for dissemination and may be responsible for late recurrence. Only powerful irradiation can combat the pelvic adenopathies. It is suggested that in the future contact roentgenograms may prove to be more efficient in this respect than present methods.

At present, it is advisable to resort to total cystectomy before the hypogastric glands become involved. The entire neoplastic organ plus the prostate should be removed, as this is the only method which offers any hope for a long survival. Only the prospect of certain death without it justifies a later operation.

Of course the prognosis of total cystectomy is rendered considerably worse when the patient has been subjected to repeated vesical incisions previously, as is usually the case. Exploratory cystotomy can frequently be avoided by cystoscopy, cystography and endoscopic biopsy. Cystoscopic examination suffices for diagnosis in 80 to 90 per cent of cases and with the aid of cystography in 100 per cent. Endoscopic biopsy should be resorted to only in the most difficult cases, and if the results are doubtful operation is indicated. Gouverneur and Dufour have used the abdominal approach in about half of their cases and in the other half a combined abdominoperineal or perineoabdominal route. With their present technic they have obtained cures in their last 5 total cystectomies.

Howard and Bergman [43] report a case of mucous adenocarcinoma of the bladder, discuss it from an etiologic viewpoint and review the recent literature. In the opinion of the writers, the tumor originated through a process of metaplasia, secondary to chronic inflammation brought on by benign hyperplasia of the prostate. Since the tumor was not located near the vesical neck and trigone, it is unlikely that it originated from the subcervical or subtrigonal glands. The tumor stripped readily and did not penetrate the muscle layers, as would be the case if it originated from urachal remnants.

Lenz, Cahill, Mellicow and Donlan [44] report the results of treatment of 44 patients with microscopically proved cancer of the urinary bladder

43. Howard, A. H., and Bergman, R. T.: Mucous Adenocarcinoma of the Urinary Bladder, J. Urol. **59**:455 (March) 1948.

44. Lenz, M.; Cahill, G. F.; Mellicow, M. M., and Donlan, C. P.: Treatment of Cancer of the Bladder by Radium Needles, Am. J. Roentgenol. **58**:486 (Oct.) 1947.

in or near the trigone. The patients were treated five to fifteen years previously with suprapubic cystotomy and implantation of radium needles (see table).

Recurrences usually manifest themselves during the first or second year after treatment. An ulcerated area should not be retreated with radium needles unless microscopic examination shows persistent carcinoma. Nonhealing radionecrotic ulcerations may develop within this period or after which cannot grossly be differentiated from recurring cancer. A dose for tumors of 8,000 gamma roentgens administered for a period of nine to ten days seemed preferable to smaller doses.

Vose and Dixey [45] report the coincidence of carcinoma of the bladder and interstitial cystitis in 3 cases. In each of these cases the symptoms and clinical findings were typical of Hunner ulcers. Each was of long standing and of such severity that the patients received little relief from the customary type of treatment. Thus when the diagnosis of

Results of Treatment of 44 Patients for Cancer of the Bladder, 1931 to 1941

Patients treated, total number	46
Died of pneumonia or coronary disease; free from cancer 2 to 4 years after treatment	2
Used for this report	44
Died of cancer—25 in 1 year, 8 in 2 years, 1 in 3 years	34
Dead in 15 years of perinephritic abscess, free from cancer at postmortem examination	1
Now alive and clinically free from cancer 5 to 15 years after treatment	9

carcinoma was made it was believed that radical treatment was indicated. Even with the addition of these cases of coincident carcinoma of the bladder and chronic interstitial cystitis to those previously reported, the total number is small. However, it is evident that it is not safe to assume that the course of chronic interstitial cystitis is entirely benign. Patients having this disease are frequently treated for long periods and should be subjected to frequent cystoscopic examinations in order that the appearance of any suspicious lesions may lead to early biopsy and appropriate treatment for malignant disease if it be detected.

Kretschmer and McDonald [46] state that in cases of carcinoma of the bladder metastasis to bone occurs more frequently than is generally appreciated. They report 8 cases of papillary carcinoma. In 1 case metastasis to bone was present although evidence of a tumor of the

45. Vose, S. N., and Dixey, G. M.: Coincidence of Carcinoma of the Bladder and Interstitial Cystitis, J. Urol. **59**:580 (April) 1948.

46. Kretschmer, H. L., and McDonald, J. H.: Carcinoma of the Bladder with Bone Metastases: A Report of Eight Cases, Surg., Gynec. & Obst. **87**:328 (Sept.) 1948.

bladder was not present at the time the patient entered the hospital. In their series the type of lesion was osteolytic. Metastasis to bone in carcinoma of the bladder occurs reasonably early in the course of the disease, and it may be the cause of the first symptoms that bring the patient to the physician. Routine roentgen ray examination in all cases of papillary tumors of the bladder may reveal the presence of metastasis to bone when least suspected.

After a brief review of the literature on tumors of vesical diverticula, Michon [47] emphasizes the fact that it is almost exclusively a disease affecting men, the ratio of men to women being 100:3. Cancer of the bladder also is commoner among males. About 100 cases of tumors in vesical diverticula have been published to date. The maximal incidence is among patients between 50 and 70 years of age. One of Michon's patients was only 46 years of age. Posterolateral diverticulum is present in most cases, frequently acquired but occasionally congenital. A few cases of tumor in urachal diverticula have been reported. The incidence of tumors in diverticula in relation to the total number of vesical diverticula is about 2 to 3 per cent.

The tumor may develop at various sites in the diverticulum, e. g., at its base, about its neck leading to strangulation or at its margin forming a sort of valve. Benign papillomas may be present as well as other vesical papillomatous lesions, and it is then often difficult to determine which is the primary lesion. However, malignant tumors are seven times as frequent as benign tumors in this location. The cancers often belong to the class of malpighian epitheliomas. Besides certain chemical substances, chronic cystitis and vesical leukoplakia may predispose to formation of tumors and are regarded by some writers as precancerous lesions. Diverticula, owing to stagnation, irritation and chronic inflammation, certainly provide such a predisposition. Most writers consider this to be the case. Hematuria is the most important and frequently the only symptom. Abundant hematuria in a patient having diverticula would suggest tumor, although infection per se may also cause bleeding.

Rectal palpation is a most important diagnostic aid since it may reveal induration in the region of the diverticula. Endoscopy and roentgenology are, however, the diagnostic mainstays. Cystoscopy will not always yield information of value; it is impossible during some stages of abundant hematuria and may lead to errors, as in 1 case in which the diverticular orifice was blocked by clots. Bleeding from the diverticular orifice is a suggestive symptom. Cystoscopic catheterization of the diverticula may yield shreds of tumor tissue. Diverticulograms may be of help. Intravenous urograms rarely are of value except to verify renal function and the ureteral relations to the diver-

47. Michon, J.: Les tumeurs des diverticules vésicaux, J. d'urol. 54:438, 1948.

ticula. Cystograms may reveal irregularities of contour or a defect in the diverticular image or a gap between the diverticula and the bladder. These images are difficult to interpret, however, and cystograms will not yield reliable information in cases in which the entire diverticulum is filled by the tumor when the diverticular orifice will not admit the opaque fluid or when the diverticulum is distended with urine. Diverticulograms yield a better picture, revealing filling defects. Electrocoagulation of the tumor is indicated rarely, and operation is the treatment of choice. Various technics of diverticulectomy have been used, that is, intravesical, extravesical or mixed, the latter two being most commonly used. Michon agrees with Hunt that the extravesical route is best, since it permits almost complete removal and diminishes the risk of dissemination. It is furthermore advisable to explore the cavity in a large diverticulum with the finger to exclude tumor before proceeding to intravesical exeresis, by submucosal cleavage.

In diverticulectomies for diverticular cancer the ureters are not infrequently injured. If a ureter has been injured, the status of renal function must be ascertained first, and if both kidneys are functioning normally implantation may be tempting. However, it is frequently impossible, owing to involvement of the ureter in the neoplastic sheath, which would require too high a section. If the patient can tolerate nephrectomy, that operation would seem indicated to avoid renal complications, and this is imperative if the suprajacent kidney is diseased (lithiasis). The most difficult cases are those in which the opposite kidney is diseased. In these cases cutaneous ureterostomy or nephrostomy would seem indicated. In cases in which the disease is far advanced, radiotherapy may be tried as in vesical cancer, though with little hope of a good result. Prognosis is the same as for vesical tumors in general. Most of the patients die within two years of operation, although in some instances survival for ten years has been reported. Three cases are reported in detail. One was a case of ulcerous infiltrating epithelioma in which the adventitial sheath of the diverticulum was involved. The second was that of a juxtadiverticular papilloma and the third that of an atypical glandular epithelioma infiltrating the neck of the diverticulum.

At present the indications for total cystectomy include infiltrating tumor of the bladder, generalized papillomatosis and recurrent neoplasm after partial cystectomy.[48] Total cystectomy has resulted in rather poor results. The mediocre results are due to poor selection of cases and use of the operation in cases of malignant disease which is too far

48. Gouverneur, R., and Aboulker, P.: La cystectomie totale chez l'homme, J. d'urol. **54**:67, 1948.

advanced, perivesical infiltration having occurred or regional lymph glands being involved. Most failures may be ascribed to use of the operation in debilitated patients having a chronic infection and compressed ureters. Integrity of one or both kidneys is an imperative prerequisite for the success of total cystectomy.

Total cystectomy requires cutaneous or intestinal diversion of the urine, either as a preliminary intervention or simultaneous with removal of the bladder. The important problem in total cystectomy is the decision on the question of successive or simultaneous performance of the two stages of the operation. Simultaneous procedure would be ideal, offering the advantage of a single operation and easier technic. Isolation of the bladder is much easier than after a preliminary operation. However, the risks involved are greater. The risk is less if an interval of two to four weeks is permitted to elapse between diversion of urine and removal of the bladder. Should complications develop after the preliminary intervention, however, the final stage of the operation may have to be delayed for weeks or months, during which time the tumor may increase in size and become inoperable. Also parietal and perivesical adhesions will then render removal of the bladder more difficult. In the future, it is to be hoped that the entire operation can be performed in one stage, namely, transperitoneal implantation of the ureters and total cystectomy.

For patients with average resistance, the chief danger of this operation is the long time required for performance, usually one and a half to two hours. Postoperative hemorrhage is insignificant, as are postoperative disturbances of diuresis. Most patients void 800 to 1,000 cc. in the first twenty-four hours. In 2 cases in which the one stage operation was performed, complete cicatrization occurred in four weeks and fifty-days, respectively. Cystoscopy is of theoretic rather than practical value. Combined with rectal palpation it will reveal the apparent discord between the limits of the tumor and the extent of vesical and perivesical induration. The posterior region of the urethra should be examined to exclude possible metastasis. Cystography is more useful. Intravenous urograms will reveal the degree of pyeloureteral dilatation and the integrity or involvement of the kidneys. Rectal and abdominal palpation, with the patient in the recumbent position and under an anesthetic if necessary, are useful aids. A search must be made for regional metastatic lesions, especially in the retrocrural glands. Endoscopic biopsy was used in only 1 case in the series.

Cystotomy is usually futile and may yield less information than cystoscopy or palpation of the bladder after the abdomen has been opened. Intravenous urograms will yield information regarding the quality of renal secretion and dilatation of excretory passages. Urograms of the ureter after release of pressure also are informative. Retrograde

ureteropyelography rarely is useful. Cystoscopic intravesical maneuvers may cause hemorrhage. If urograms reveal good function of both kidneys, the two ureters can be implanted transperitoneally simultaneously. This was done in 21 cases, and in 2 cases in which there were three ureters all three were implanted. If urograms show poor function in one kidney, the ureter on the normal side is implanted into the intestine and the one on the abnormal side is implanted into the skin, in preparation for nephrectomy later. If the patient has only a single kidney, the ureter can be implanted by the peritoneal or subperitoneal route. This was done twice successfully by the authors. Often the decision as to whether or not to implant must be made during the operation, after the condition of the canal is seen and its dilatation and flexibility are determined. Its elasticity is a more determining factor than the state of dilatation. A rigid ureter of any caliber is less suited for implantation than a more elastic dilated ureter. If liberation of the ureter proves difficult or causes small hemorrhages, the advisability of implantation is diminished. The success of intestinal implantation of the ureter depends on perfect technic more than any other urologic operation. The authors use the Coffey no. 1 technic, with slight variations and without a ureteral catheter. After preparing a good intestinal bed, care must be used to avoid any kinking or constriction of the ureter, which lies in its submucosal tunnel, without other fixation than the stitch attaching it to the intestine.

In cases of inoperable tumors, implantation of the ureter places the bladder at rest and greatly improves the general condition of the patient. These patients often believe themselves cured, and their survival is greatly prolonged.

In 21 cases intestinal implantation of the ureters was done preliminary to total cystectomy (in all forty-two implantations; two on three ureters, seventeen on two ureters and two on one ureter). Death was not attributable to the anastomosis in any case. Late ureterocutaneous fistula without urinary peritonitis occurred in only 2 cases. In the interval between derivation and cystectomy, the bladder is irrigated and penicillin instilled.

Gouverneur and Aboulker [45] used the abdominal route most frequently. Perivesical infiltration is a contraindication to the operation. The operation begins with a retrosymphysial liberation of the anterior surface of the bladder and the prostate, followed by ligature of the preprostatic veins and lateral detachment. The peritoneum is opened at the beginning of the operation, for detection of adhesions to the intestine or omentum and invasion of the iliac glands. The peritoneal cap is detached from the dome of the bladder and carefully closed in two layers. Anterior detachment is then resumed, the ureter being divided at

the beak of the prostate, which is grasped with forceps and lifted up and forward. The bladder is then detached from the rectum, and the lateral pedicles are ligated. Sulfonamide powder is blown into the cavity, and a hypogastric drain is inserted.

A preliminary liberation of the prostate as suggested by Albarran facilitates removal of the bladder. Gouverneur and Aboulker have used this combined perineal-abdominal route in several cases but feel that the advantages gained do not compensate for the inconveniences encountered. The operation becomes too complicated and requires a change in position of the patient during the operation, which interferes with asepsis and takes valuable time. Then, too, exploration of the abdomen after liberation of the prostate might reveal conditions contraindicating cystectomy, which would then have to be performed, even though futile. Also, after cystectomy the proximity of the anus carrying the drain from the intestinal diversion adds the risk of infection of the perineal incision. Perineal liberation is superfluous after high section of the ureter with traction on the prostate. Thus it is the intestinal implantation that offers difficulties rather than removal of the vesicoprostatic mass.

The unfavorable psychologic effect of repeated operations for tumors of the bladder and the time lost between diagnosis and removal of malignant tumors by preliminary operations have led Iglesias de la Torre [49] to attempt a single stage, combined operation including transplantation of the ureters into the sigmoid, with total cystectomy and panhysterectomy in women and abdominoprostatoseminal vesiculectomy, including a large portion of the vas deferens and membranous urethra en bloc, in men. In women, cystectomy is facilitated by ligature of the hypogastric arteries. The disadvantages of current methods of ureteral implantation are discussed. The following technic was used in 50 cases without a single failure.

After preliminary preparation of the patient, which includes transfusions of blood (as many as twenty if necessary), administration of folic acid, vitamins and liver extract and the bringing of blood proteins and blood urea up to normal concentrations, a median infraumbilical incision is made which continues up to 2 inches (5.08 cm.) above the umbilicus with the patient under endotracheal anesthesia. The intestine is thoroughly evacuated and treated for several days before operation. Shortly before operation the bladder is irrigated with a solution of potassium permanganate, and a solution of penicillin is instilled. The leaves of the mesosigmoid are dissected and the ureters liberated by

49. Iglesias de la Torre, J.: Cistectomía total con implantación de los uréteres a la sigmoide en un solo tiempo en los tumores infiltrantes de la vejiga, Arch. cubanos cancerol. **6**:317 (Oct.-Dec.) 1947.

blunt dissection, after which ligature of the hypogastric arteries is performed if the patient is a female. These peritoneal membranes are used later to cover the site of implantation, after immobilization of the intestine at this point to prevent peristaltic traction on the ureter.

After careful preparation the ureters are implanted, the right slightly below the left. The ureters should be cut obliquely to avoid invagination, edema and spasm. Even transitory compression of the ureter must be avoided. Double ureters are implanted as one. Dilatation or enlargement of the ureter is not a contraindication to implantation. A dilated ureter with nonpurulent content may be implanted immediately after mobilization. If the content is purulent, irrigations with saline and penicillin solutions are recommended. The ureters must not be held too tense or too lax. Only a single layer of sutures is used (not exceeding four). The ureter is fixed with a nonperforating suture at the inferior margin of the superior angle of the intestinal incision, and before the ureter is buried in the intestine a sound is passed to insure free drainage and to be sure that the sutures are not causing any compression. After ligature of the hypogastric arteries in the female a panhysterectomy is done, and in the male the radical abdominoprostatoseminal vesiculectomy described previously is performed.

Immediately after operation, the patient is placed in the Fowler position, and infusion of dextrose solution with penicillin is continued for three days. Fluids by mouth are permitted from the third day. The abdomen should be immobilized for six days, with the aid of morphine if necessary. Every third day 500 cc. or more of plasma is injected. Patients are encouraged to cough, breathe deeply and move their extremities to prevent vascular and pulmonary complications, and are usually able to get up after two or three weeks. The technic of the operation is described in detail, with fifty illustrative figures in the complete paper.

Hoyt [50] reports a case of cystitis cystica which occurred as a single tumor in a Negro woman 36 years of age. The tumor measured 4 by 4 by 2 cm. and was attached to the vesical wall over its entire area. About 10 Gm. of tissue was resected transurethrally and the base coagulated. Microscopic sections showed structure typical of cystitis cystica. This condition may occur as a single tumor or as multiple tumors of considerable size in the bladder. Cystitis cystica, cystitis glandularis, cystitis follicularis, cystitis emphysematosa and leukoplakia are all somewhat similar processes of proliferation of cells, and it is suggested that they may be classified together.

50. Hoyt, H. S.: Cystitis Cystica as a Single Tumor, J. Urol. **59**:424 (March) 1948.

Fistula.—Counseller [51] states that 99 per cent of all vesicovaginal fistulas observed at the Mayo Clinic are repaired by the vaginal approach. Many of the patients are placed in the Kraske position because the vaginal vault falls forward and the fistula is readily identified and approached surgically. In mobilizing the bladder the surgeon should incise the vaginal wall well above, below and around the fistula. The entire urethra, trigone and base of the bladder can be exposed if necessary. The cul-de-sac of Douglas is opened to explore the pelvic cavity and to separate any portion of the small bowel or sigmoid from the bladder. The bladder can then be pulled more into the vagina, and all scar tissue around the fistula excised. The defect in the bladder is closed in layers either anteroposterior transversely or diagonally, depending on direction and shape of the fistula. The author recommends absorbable suture material. The first row is made with chromic surgical gut no. 000, the second with no. 00 and the third with no. 0. The vaginal mucosa is closed with interrupted sutures of chromic surgical gut no. 1. After operation the patient is placed on a Bradford frame for two weeks. The catheter drains directly into a small basin, and it is irrigated frequently to prevent plugging. The urine is acidified. Vaginal examinations are deferred until one week after the patient leaves the hospital. Counseller discusses the etiology and prevention of vesicovaginal fistula and emphasizes the importance of complete urologic study before a repair is attempted once a fistula occurs.

Rupture.—Jåfs [52] describes a case of rupture of the urinary bladder due to some movement in the patient's work or possibly to strong miction with a distended bladder. The patient had not been injured, and pathologic changes were not noted in the walls of the bladder. He had consumed alcoholic drinks before the rupture occurred. After surgical repair of the rupture, he made an uneventful recovery. Results of cystoscopic study were negative.

Experimental Study.—Rubin [53] reported that the formation of an artificial bladder from a portion of the sigmoid has been successfully performed experimentally in 7 dogs, with satisfactory results. Ascending renal infection has not been evident in the dogs seven and a half months after operation. Infection of the new sigmoid bladder can be effectively brought under control by adequate antibiotic therapy. The new bladder is accessible to instrumental and diagnostic examination as well as to

51. Counseller, V. S.: Etiology, Prevention and Treatment of Vesicovaginal Fistula, South. Surgeon. **13**:752 (Oct.) 1947.

52. Jåfs, R.: En blåsruptur, Nord. med. **35**:1633 (Aug. 1) 1947.

53. Rubin, S. W.: The Formation of an Artificial Urinary Bladder with Perfect Continence: An Experimental Study, J. Urol. **60**:874 (Dec.) 1948.

suprapubic exploration without contamination of the field. Reasons why this procedure should not be attempted in human beings have not been found, especially when infiltrating neoplasia of the bladder is being treated. With this procedure, a bladder can be obtained which exhibits perfect control of the passage of urine through the urethra. Clinically, the operation may be performed on human beings as a one stage procedure. An original experimental study on dogs has been presented wherein for the first time a one stage operative procedure was performed in order to construct an artificial urinary bladder out of a loop of sigmoid excluded from the continuity of the colon. Both ureters were inserted into this new bladder, and then the bladder was anastomosed to the urethra in order to establish continence and urinary control.

Drainage.—Boyd [54] uses cystotomy to treat patients who have disturbances of micturition accompanied with acute injuries to the spinal cord except in cases of lesser injuries with transient disturbances of micturition.

Suprapubic drainage can be temporary or permanent, depending on the extent and duration of the disturbance of the bladder's function and also on whether or not adequate function can be restored by transurethral resection of the neck of the bladder. Automatic micturition and most of the other types of abnormal micturition from which these patients later suffer rarely should be permitted to continue. Cystotomy should be performed at once in nearly all cases of paralysis in which it is likely that disturbances of micturition will continue for more than six or eight weeks. The benefits of cystotomy are (1) adequate urinary drainage which avoids overdistention of the bladder and permits good control of infection of the bladder by irrigation and urinary antiseptics and (2) freedom from trauma to the urethra by catheter and from urethral and periurethral infections, prostatitis, seminal vesiculitis and epididymitis.

Attendants find it much easier to care for patients at home who have undergone cystotomy than for those having unsatisfactory types of abnormal micturition or intermittent or continuous catheterization.

Incontinence.—Marshall and his co-workers [55] describe the correction of stress incontinence by vesicourethral suspension. In this procedure a number of sutures are placed lateral to the urethra, and three sutures are also placed laterally on the wall of the bladder. These

54. Boyd, M. L.: The Advantage of Suprapubic Drainage over Catheter or Other Methods of Urinary Drainage in Acute Bladder Paralyses Which Result from Traumatic Injuries of the Spinal Cord, J. Urol. **60**:922 (Dec.) 1948.

55. Marshall, V. F.; Marchetti, A. A., and Krantz, K. E.: The Correction of Stress Incontinency by Simple Vesicourethral Suspension, Surg., Gynec. & Obst. **88**:509 (April) 1949.

sutures are then tied to the pubis and rectus muscles. This gives elevation and immobility of the vesical neck and urethra. Among 44 suitable cases excellent results were obtained in 36, or 82 per cent. Some improvement was shown in 7 per cent and no improvement in 11 per cent. It is not the intention of the authors to advocate this operation to the exclusion of others. They emphasize the following two principal points: 1. Elevation and fixation of the vesical neck is a major factor in the maintenance of urinary control. 2. This operation is worthy of trial in selected cases in which previous operation has failed.

Hayes [56] discusses urinary incontinence after perineal prostatectomy and recommends suture of the levator ani muscles for absence or weakness of the internal sphincter muscles. This is an easy operation and is successful. In the female urethra it cannot be done, but the fibers making up the vesical neck and floor of the bladder are thick enough so that with careful dissection they can be brought forward to make a sphincter that is effective. Hayes reports 2 cases in which this type of operation was performed, with good results in 1 and fair ability to control the urine in the second.

PROSTATE

Surgical Procedures.—Questionnaires [57] were sent out to prominent European urologists inquiring as to their preference for transvesical, retropubic or endoscopic removal of adenoma of the prostate and their reasons for such preference, with statistical confirmation of their opinions when possible. The twenty-three replies show that, with the exception of three surgeons who had had insufficient or no experience with the Millin operation, all were highly enthusiastic over the results obtained with this new technic, their collected statistics including some 568 cases, with a mortality rate of nearly 3 per cent. Weijtlandt, of Amsterdam, has employed the retropubic (Millin) operation in 39 cases up to the time of this report with only 1 death, or a mortality rate of 2.5 per cent. Pisani, of Milan, employed various technics for comparison, having used the Fuller-Freyer technic in 3,000 cases, the perineal route in 100, the Hay operation in 20, the Millin operation in 30 and the endoscopic technic in 200. He obtained good functional results from all technics. Pain, risk and trauma were all greater with the Fuller-Freyer technic, and recovery was slower when this method was used. The perineal operation was far less traumatizing and presented the advantage of leaving an anatomically perfect urethral canal. Its chief disadvantage was postoperative impotence. The Hay technic

56. Hayes, B. A.: The Treatment of Urinary Incontinence, J. Oklahoma M. A. **40**:482 (Dec.) 1947.

57. Discussion: Techniques d'adénectomie prostatique, J. d'urol. **54**:237, 1948.

yielded good results in aseptic cases in which the prostate was not too large. Use of this method did not result in any deaths, and recovery was rapid. At present, Pisani considers that the Fuller-Freyer technic is indicated only for rare cases of diverticulum, large calculi, tumors and so forth. In septic cases involving elderly and debilitated patients, he considers the perineal route the best, because there is minimal trauma, but for the great majority of cases he prefers the Millin technic.

Suter has used the Millin operation in only 15 recent cases and therefore cannot at this time express his opinion on its comparative value. In 316 cases of transvesical adenectomy his mortality rate was 4.4 per cent when the operation was done in one stage. In cases of renal and cardiac disease the two stage operation was used. He employed transurethral electroresection in 648 cases, with a mortality rate of 1.6 per cent. This procedure is indicated for less marked hypertrophy and atrophy and for patients who can tolerate only one major operation or for those whose renal and general condition constitutes a contraindication to prostatectomy. Electroresection requires considerable cystoscopic experience and patience, and the postoperative treatment is longer and more complicated than after prostatectomy or the Millin operation. Joly, of London, knew nothing of the Millin operation. He always preferred transvesical adenectomy by the Thomson-Walker technic or the simple Freyer enucleation. He abandoned the perineal route owing to the grave risk of incontinence and employed the endoscopic route for cancers and fibrous prostates, because he believed it impossible to accomplish complete removal of the adenoma by the transurethral operation. Keller, of Copenhagen, who has not had any experience with the Millin operation, has abandoned the perineal operation and considers the simplest technic to be that of the Freyer operation. The two stage procedure is employed only in cases of severe retention. The endoscopic route is reserved for dysectasias of the vesical neck but never for real hypertrophy, in which it has only a palliative effect and is accompanied with the same risk as a transvesical operation. Perrier, of Geneva, uses the Millin operation exclusively, in one or two stages, and finds that it has all the advantages and none of the disadvantages of the Freyer operation. It is also possible in cases in which use of the Freyer operation would be contraindicated. The Millin operation is longer and more difficult than the Freyer operation, but the results justify the use.

Stobbaerts has used the Millin procedure in 51 cases since 1946, with 3 deaths, 2 due to embolism and 1 to shock. He continues to use the endoscopic technic for small adenomas and acquired or congenital anomalies of the vesical neck.

Boretti, of Milan, has employed the Wildbolz perineal adenectomy since 1942. He uses transurethral endoscopic resection for small

adenomas of the median lobe, bars and lesions of the vesical neck. He urges individualization in selection of technic, has not had any experience with the Millin operation and reserves the perineal operation for obese patients and men more than 65 years of age. For all cases in which infection and complications are present and for large trilobar adenoma he employs the transvesical route.

Nora, of Paris, does not use the perineal operation but only transvesical, retropubic or endoscopic resection. In 294 cases of transvesical adenectomy, he had 6 deaths, or a mortality rate of 2 per cent, and his patients were kept in bed for from twenty-three to thirty days. One in 20 will require repacking for hemorrhage. Functional results are good. Partial retention is common in the early postoperative period but responds to the use of lavage and dilation. The urine clears in six weeks to two months.

Nora is of the opinion that the Freyer operation is and will remain a satisfactory procedure and that it will lead to decided improvement in the general condition of the patient and to the return of libido. He does not advocate the use of the endoscopic route, which he believes should be reserved for adenomas of the median lobes, for small cervical adenomas or for cachectic patients, in an effort to avoid a poorly tolerated cystostomy. Death from operation seldom occurs, if ever, and the immediate results are good. He had performed only twenty-seven Millin operations and used the Marion modification. He expresses the opinion that the Millin operation has a good future but states that it would be unwise to extend its indications at present beyond those now stipulated for the Freyer operation.

Since the advent of the Millin operation, Gouverneur and Aboulker have revised their indications and choice of surgical procedure. They give the extravesical technic first choice since it permits visual control, has few postoperative complications, does not give rise to urinary fistulas and renders secondary closure of the bladder superfluous. They emphasize, however, the need for careful supervision of the patient for the first two or three days after operation, with constant attention to the catheter and to irrigation and aspiration if they are necessary. The physician also must watch for bleeding. Avoidance of fistulas will depend on careful closure of the bed. The urine usually clears up in thirty to forty-eight hours. Large adenomas, up to 145 Gm., have been removed successfully by this method, with no signs of bleeding during or after operation. Good cicatrization depends largely on the patient's vitality and resistance. Gouverneur and Aboulker recommend the Freyer operation for patients having renal deficiency, stubborn chronic retention and poor general condition. It also is recommended when azotemia is persistently high in spite of dietary precautions and an indwelling catheter. Cystostomy will be required in cases of chronic

retention, which injures the parenchyma and causes urinary infection. In such cases the catheter must be left in place for a long period. Endoscopic resection is reserved for lesions of the vesical neck and for small adenomas. The results of resection never are as perfect as those after adenectomy. The perineal operation has rare but definite indications. It is useful in debilitated and obese patients having large prostates and proves beneficial in some cases in which no other operation is indicated.

Duvergey, of Bordeaux, now uses the Millin technic in 75 per cent of his cases. The mortality rate of this operation ranges from 4 to 8 per cent, and complications occur in 26 per cent. Duvergey reported 3 deaths in his series of 50 cases. He feels that routine employment of the Millin technic would be a mistake but recommends its use for cases of noninfection, the endoscopic procedure being reserved for small adenomas. Cystostomy as a first stage of adenectomy is only rarely indicated. The Millin operation is indicated in the earlier stages before infection has developed.

Macquet, of Lille, prefers the Millin operation, reserving the transvesical procedure for patients with debilitation, renal disease or infection. The endoscopic route is recommended only for stenosis of the vesical neck and not for adenoma of the prostate. It does not permit complete removal of the adenoma, visual control or adequate hemostasis. The perineal operation is followed by fistula, incontinence and sexual impotence. Only the retropubic operation yields full satisfaction. Hypogastric fistula may be avoided by more careful burying of the sutures. The indwelling catheter may be removed on the third day, which will reduce the number of complications. Macquet had done sixty Millin operations at the time he reported, with only 2 deaths neither of which could be attributed directly to the operation. René-Henri Martin, of Paris, uses the retropubic route almost exclusively, having done seventy-one operations by this technic since January 1947.

Viollet, of Limoges, has used the Millin operation since October 1946, having done seventy operations, with a mortality rate of 6 per cent in the first 34 cases but of only 3 per cent in the last 36 cases. In cases in which cystostomy has been done, he prefers the Freyer to the Millin operation. Martin-Laval, of Marseilles, has not had experience with the perineal or Millin technics. He uses endoscopic resection for lesions of the vesical neck or prostatic bar only and transvesical prostatectomy for hypertrophy. His mortality rate with the latter operation has been 4 to 5 per cent. Frédet, of Chartres, while admitting that patients and surgeons demand the Millin operation, feels that it should not be regarded as a panacea but only as an additional weapon. He has not completely abandoned the transvesical and endoscopic procedures. He prefers the Freyer operation in two stages. In his series

of thirty-eight Millin operations 2 deaths occurred; 1 death was due to pulmonary complications in an aged patient, and the other patient had carcinoma and died the day after operation.

Dufour, of Paris, recommends the endoscopic operation for adenomas of less than 20 Gm. He states that only Young obtains good results with the perineal operation. If the bladder is distended and infected, he does a two stage transvesical operation for large adenomas. He recommends the Millin operation for the great majority of patients.

Truc, of Montpellier, finds the greatest advantages of the retropubic operation of Millin to be visual control and good hemostasis. However, it is difficult and complicated. If clotting and evacuation cannot be controlled by irrigations, cystostomy may be required. He does not advise routine application of the Millin technic because of the danger of fistula, hemorrhage and cellulitis and possible postoperative incontinence. It should be used only in cases of noninfection. One patient of his first 16 who underwent the Millin operation died from embolism on the third day. He feels that his experience with this technic has been too limited to permit an evaluation and states the belief that the transvesical route is still justified.

Sabadini, of Algiers, has done only Millin operations since 1945. In all, he performed ninety such operations, with only 3 deaths. One of these was due to cellulitis, furunculosis, which occurred preoperatively, having been ignored and penicillin not having been administered preoperatively. The second death was due to heart failure on the night after the operation, and the third death was due to shock which began while the operation was being performed. The present day use of antibiotics should greatly improve results. Sabadini is of the opinion that nothing is to be gained by removing the catheter before the eighth or ninth day. His results with the modified Millin technic have therefore been excellent.

Chauvin, of Marseilles, has rejected the perineal route of operation. In most of his cases he employs Freyer's transvesical enucleation. He considers the Millin operation more dangerous than the Freyer operation and reserves the former for his most favorable cases. Laffitte and Suire, of Niort, have used the Millin technic since 1947. No deaths occurred in their 43 cases; complications occurred in 6 cases. Complications included phlebitis, pelvic phlebitis, pneumonia, cerebral ischemia and imperfect drainage. Laffitte and Suire consider the Millin procedure the operation of choice for adenoma. It must be used with greatest precaution if adenoma is associated with lithiasis and hematuria. Tachot, of Pau, always had such good results with the Freyer operation that he hesitated to try the Millin technic. However, the long time required for the latter and its difficulty is more than compensated for by the reduction in postoperative hemorrhage. He considers the

greatest advantage of the Millin technic the suppression of vesical contractions, which are partially responsible for hemorrhage and immediate postoperative sequelae. Bilger, of Strasbourg, definitely prefers the Freyer operation to the Millin procedure. He considers it premature to remove the catheter on the third day. The Millin operation, in his opinion, definitely is not superior to the Freyer operation in two stages, which can be used for debilitated or infected patients and has a mortality rate of only 2 per cent although it requires hospitalization for eight to ten days longer than the Millin operation.

Gorday [58] states that prostatic operation has become less hazardous for the aged and can be performed with a relatively low mortality rate. Factors involved in the changing concept of prostatic operations for the aged include (1) reduction of mortality rates through increased experience with technics of transurethral resection; (2) adaptability of transurethral resection to treatment of carcinoma of the prostate, which increased the number of aged persons now accepting operation; (3) critical analysis by advocates of other forms of prostatic operations which led to improved technics to rival the results of resectionists; (4) discovery and use of the newer antibiotics, and (5) recognition of the value of a cardiac consultation preoperatively. In a series of 132 cases of prostatic obstruction in which operation was performed 19 patients were over 75 years of age. The general mortality rate for transurethral resections was 2 per cent and for suprapubic prostatectomy, including 2 patients who did not reach the second stage of operation, 9 per cent. Six aged patients were treated by two stage suprapubic prostatectomy, with 1 death. One patient, 78 years of age, died of coronary occlusion before the second stage could be performed. Fourteen resections were done on 12 patients over 75 years of age, with no deaths.

Retropubic Prostatectomy: Badelon, Renon and Rautureau [59] divide their series of 17 patients who underwent Millin prostatectomy into two groups, namely, those with indwelling catheters at the time of operation and those without them. The results in the first group of patients, whose ages ranged from 56 to 73 years, were satisfactory. The patients were allowed to be up from the fourth to the eighth day, the catheter was removed any day from the eighth to the eleventh and they were discharged any time from the twelfth to the twenty-eighth day after the operation. The second group was comprised of older patients ranging in age from 72 to 84 years, the average age being 75 years. In this group results were not so good. There were 2 early

58. Gorday, A. J.: Prostatectomy in Men Over Seventy-Five, J. Urol. **59**:708 (April) 1948.

59. Badelon, P.; Renon, C., and Rautureau, M.: A propos de la prostatectomie estravésicale: Intérêt de l'uréterographie post-opératoire, J. d'urol. **54**:280 (Feb.) 1948.

deaths, even though rising and removal of the catheter had been delayed. Hospitalization in this group was longer because of pulmonary, cardiac or uremic complications. There was 1 late death on the twenty-seventh day, and 1 failure occurred. Patients with reduced vesical capacity and stubborn urinary infection are not fit subjects for the Millin operation. The complications included transitory suprapubic fistula responding to catheterization in 3 cases; in 1 this developed after suprapubic adenitis and in the other 2 after severe retropubic suppuration. One patient continued to have slight incontinence, and another had unsatisfactory control of the sphincter.

The end results were satisfactory on the whole. The authors emphasize, however, the delay in return of normal vesical function. Frequency occurred in some, and 3 patients had a filiform jet, in spite of normal caliber, and stubborn infection. The residual urine was from 10 to 130 cc. Urograms (retrograde) showed poor function of the smooth sphincter, which emitted only a tiny jet of opaque fluid. This suggested sclerosis involving the segment close to the site of enucleation. A pseudoneoplastic appearance suggested reflex spasm of the smooth sphincter or massive sclerosis of its tissues. The condition apparently is not related to resection of the posterior lip of the vesical neck. A certain degree of urinary infection was not uncommon in this particular form of dysectasia, possibly due to postoperative cicatrization. Surgical injury, near the smooth sphincter, might have disturbed function, giving rise to pollakiuria with stagnation, as observed. It is not impossible that dysfunction of the vesical sphincter might have been responsible for vesical atony with retention in 2 patients and for the late death of 1 of them.

Millin's technic for retropubic prostatectomy has stimulated urologists to renewed efforts and originality. So many modifications of Millin's technic have been suggested that the operation rarely is performed as originally planned by him. Perineal prostatectomy seldom is used in France. Cibert [60] advocated the Freyer technic and was at first unimpressed by the Millin technic. However, after seeing the operation performed by Couvelaire and being convinced of its simplicity and favorable results, he has now used it in more than 300 cases. The mortality rate averaged 6 per cent (8 per cent for the first 100 cases, 7 per cent for the second 100 cases and only 3 per cent for the last 100 cases), which is lower than the rate obtained with the Freyer operation. Also, by means of the Millin technic Cibert was able to extend the limits of operability and could operate on patients for whom a transvesical or transurethral operation would have been contraindicated. The most frequent complications were leakage of urine through

60. Cibert, J.: La chirurgie urinaire rétropubienne selon Millin (d'après 300 observations), J. d'urol. **54**:207 (March 11) 1948.

the wound in the hypogastrium, fistula and suprapubic leakage. However, the fistulas were not serious and many healed spontaneously; in most cases catheterization was required for a few days only. Hemorrhage occurred in 21 cases, in 5 cases on the first day, in 2 on the second day and in 14 from the sixth to the thirty-third day. Other complications included orchitis in 18 cases, myocardial infarction in 1, pulmonary complications in 9, pubic osteoporosis in 1, pubic osteitis in 1, phlebitis in 6, pulmonary infarct in 1 and some attacks of pyelonephritis. Incontinence in the immediate postoperative period occurred in 16.66 per cent of the cases. Some of the patients recovered spontaneously, and others required dilation or nerve infiltration. In 6 cases incontinence persisted, in 2 owing to constriction of the membranous urethra.

No other operation has given Cibert as favorable results as the Millin operation. Millin has proved that the principles which made a success of endourethral surgery, that is, preliminary introduction of the indwelling catheter, removal of the prostate without urinary diversion and direct hemostasis, are applicable also to open operation. The facilities furnished by the Millin operation for complete enucleation and perfect hemostasis give this procedure first place among available technics.

Morville [61] reports his experience in performing retropubic prostatectomy after the surgical technic of Millin. The advantages of the operation are (1) safe and easy extravascular approach to the prostate; (2) easy enucleation of the gland; (3) good vision of the operative field, which reduces the chances of leaving prostatic calculi, isolated small adenomas and tissue remnants which might become necrotic; (4) control of bleeding by ligation of vessels; (5) reduction of secondary hemorrhage and serious postoperative infection by suture of the prostatic bed above the catheter; (6) much less shock as compared with suprapubic prostatectomy, and (7) smooth convalescence requiring less nursing care.

Bacon [62] states that retropubic prostatectomy is anatomically sound as important organs are not disturbed or endangered. All obstructing tissue is removed, which thereby eliminates the risk of recurrence. There is practically no danger of postoperative or delayed hemorrhage or of persistent fistula, prolonged infection or urethral stricture. However, the procedure is done in a highly vascular region, so that exact and prompt ligation of precapsular veins must be carried out. Retropubic

61. Morville, P.: Retropubisk prostatectomi a. m. Millin, Nord. med. **35**:1623 (Aug. 1) 1947.

62. Bacon, S. K.: Retropubic Prostatectomy: An Extravesical Technique: Report of Thirty-Two Cases, J. Urol. **59**:376 (March) 1948.

prostatectomy is an efficient operation, the postoperative period relatively short and progress remarkably gratifying. It avoids the disasters and indignities (rectourethral fistula, incontinence and impotence) of perineal prostatectomy. It is not applicable to prostatic fibrosis, contracture of the vesical neck or extensive carcinoma. The author reports briefly on 32 cases.

Transurethral Prostatic Resection: Greene and Heck [63] report on a series of 40 patients with various types of blood dyscrasias who underwent transurethral prostatic resection. The majority of these patients had pernicious anemia, but those with chronic myelogenous leukemia, chronic lymphatic leukemia, hemophilia, polycythemia vera and hemolytic icterus are included. The fact that death did not occur after surgical procedure in any case indicates that the surgical risk is not high when proper treatment is provided during the preoperative and postoperative periods. With the exception of hemophilia, postoperative convalescence is similar to that of patients who do not have blood dyscrasias, and the functional results of operation are equally good. In every case examination of prostatic tissue removed at operation disclosed benign adenofibromatous hyperplasia. In 1 case of chronic lymphatic leukemia dense lymphocytic infiltration was present. It is a singular fact that no instance of prostatic carcinoma was encountered, inasmuch as normally 6 to 8 cases of carcinoma would be expected in a group of this nature.

Creevy [64] states that hemolysis of blood, such as occurs in curing blackwater fever and after transfusions with incompatible blood or after severe burns, leads to hemoglobinemia and hemoglobinuria. Severe hemoglobinemia may damage the kidney by producing spasm of its vessels, by a direct toxic action on the tubular epithelium and by the production of pigmented casts which plug the nephron. Intravesical and intravascular hemolysis may be produced during transurethral prostatic resection by water used as an irrigating fluid. Hemoglobinemia probably does not harm the kidney unless (1) the hemolysis is severe, (2) the kidney is simultaneously damaged by vasospasm from excessive loss of blood or by surgical shock or (3) virulent bacteria are transported from the prostate to the kidney by the irrigating fluid. A hemolytic reaction may be recognized at once by measuring the free hemoglobin in the plasma at the end of the operation. This is recommended as a routine procedure with transurethral resection if water is used for irrigation. The reaction itself is characterized by chills, nausea, oliguria,

63. Greene, L. F., and Heck, F. J.: Transurethral Prostatic Resection in Cases of Blood Dyscrasias, J. Urol. **60**:247 (Aug.) 1948.

64. Creevy, C. D.: The Importance of Hemolysis During Transurethral Prostatic Resection: A Clinical Investigation, J. Urol. **59**:1217 (June) 1948.

rising urea nitrogen, mild jaundice, anemia out of proportion to the amount of blood actually lost during and after operation and, at times, a late rise in blood pressure. The hemoglobinuria is masked by the usual postoperative hematuria. Forcing of fluids during and immediately after operation may aid in excretion of the hemoglobin with less damage to the kidneys, but after oliguria has appeared one must be cautious in administering fluids. Otherwise, treatment consists in trying to keep the patient alive until sufficient time has elapsed to permit recovery of the damaged renal epithelium. Peritoneal lavage may be of some value in achieving this end.

Hemolytic reaction can be prevented by using an isotonic solution of a poor electrolyte, such as 4 per cent dextrose, as an irrigating fluid during transurethral resection of the prostate. A fatal reaction is reported in a case in which sterile water was the irrigating agent. Anorexia, hemoglobinemia, anemia, jaundice, uremia and hypertension occurred. Peritoneal lavage brought about a remarkable reduction in the urea nitrogen without diuresis, but death occurred from pulmonary edema. Clinical studies have shown that water, when used as an irrigating solution during transurethral resection, does produce hemolysis which may be severe enough to cause uremia and that hemolysis does not occur when isotonic solution of dextrose is used. Evidence is presented of extensive absorption of glucose during operation. The use of an isotonic solution for irrigation during transurethral resection has resulted in a striking reduction of morbidity and mortality.

Nesbit and Glickman [65] state that the irrigating solution employed in transurethral resection of the prostate may pass directly into the prostatic veins and result in hemolysis of varying degrees. Excessive hemolysis from such a cause in conjunction with operative shock or marked loss of blood acting on kidney damage by chronic pyelonephritis or arteriosclerosis or by a combination of the two diseases may result in a clinical syndrome manifested by anemia, oliguria or anuria and uremia. This syndrome may end fatally. The phenomenon due to this cause can be prevented by the use of any isotonic nonelectrolytic irrigating solution. A 2.1 per cent solution of amino-acetic acid, while not isotonic, has been found to satisfy the proposed criteria; it has been employed successfully in forty-five transurethral prostatic resections without demonstrable gross evidence of intravascular hemolysis. A 1.1 per cent solution of amino-acetic acid, while not isotonic, has been found to be nonhemolytic in vitro and has been used in thirty resections without producing hemolysis. The use of the lower concentration is economical as well as safe, so its employment as an irrigating solution during transurethral prostatic resection is advised.

65. Nesbit, R. M., and Glickman, S. I.: The Use of Glycine Solution As an Irrigating Medium During Transurethral Resection, J. Urol. **59**:1212 (June) 1948.

McLaughlin, Bowler and Holyoke [66] present an analysis of 16 fatalities after transurethral resection of the prostate gland. More than half of these deaths were due to factors over which the resectionist had direct control. In order to reduce the mortality rate from prostatic resection, the technic of resection must be better understood and applied. The use of prophylactic antibiotics and chemotherapy before, during and after resection should materially reduce the incidence of death due to sepsis. Early mobilization of patients and the use of active exercises for the legs of patients who are bedridden would appear to be the most effective means of lowering the number of fatal pulmonary emboli due to thrombosis of the veins of the leg. The use of isotonic irrigating solution or the judicious use of sterile water during resection should reduce the incidence of the oliguria syndrome.

Griffin [67] discusses toxic symptoms after transurethral resection. In a series of 194 cases of transurethral prostatectomy, the symptom complex of nausea, vomiting and rise in blood pressure was noted five times. The cause of these symptoms was attributed to the entrance of irrigating water into the prostatic veins, because the occurrence of the symptoms in each instance was simultaneous with attempts to control venous hemorrhage and the patient's blood plasma, in each case, revealed hemolysis postoperatively. Hemolysis after transurethral resection was found by routine examination to have occurred frequently in other cases without subjective complaint or recognized symptoms. The five patients who exhibited toxic symptoms did not have permanent ill effects. The observations reported indicate that some substance poorly tolerated by the patient was liberated in the process of hemolysis or some toxic agent was introduced into the blood stream in the irrigating water, which was responsible for the toxicity with the amount of hemoglobin liberated in the plasma. The literature concerning hemoglobinemia, particularly as regards blackwater fever and reactions from transfusions of blood, indicates that renal failure as a result of tubular degeneration, with or without plugging of the nephron with hemoglobin casts, is often the primary cause of death. A series of 328 consecutive cases of transurethral prostatectomy is reported in which only 1 of the 3 deaths was due to renal failure. Postoperative shock resulting in renal ischemia, not a postoperative hemolytic reaction, was considered to be the cause of renal tubular degeneration in this case. The use of isotonic irrigating solution to prevent hemolysis during transurethral prostatic resection must be carefully evaluated or the remedy may be worse than the fault

66. McLaughlin, W. L.; Bowler, J. P., and Holyoke, J. B.: The Causes of Death Following Transurethral Resection of the Prostate, J. Urol. **59**:1233 (June) 1948.

67. Griffin, M.: Toxic Symptoms Accompanied by Hemolysis During Transurethral Prostatectomy, J. Urol. **59**:431 (March) 1948.

it is designed to correct. Isotonic saline solution can be and has been used by the author while operating with the Thompson resectoscope, but the diffusion of the current through the electrolytic solution requires a stronger current for coagulation, and the electrode must be placed more accurately on the bleeding vessel. The danger of upsetting the blood chemistry of patients who are poor surgical risks must be carefully evaluated in selecting a substitute for water as the irrigating medium. For this reason, dextrose is preferred to sodium chloride in preparing irrigating fluid for patients having severe cardiovascular disease. At least for the present, the most important precautions to be taken in prevention of hemolysis during transurethral prostatectomy are to leave a rim of prostatic tissue between the line of dissection and the prostatic capsule until the final moments of the operation and to use irrigating water at the lowest workable pressure.

Emmett and Beare [68] discuss transurethral resection for vesical dysfunction in cases of tabes dorsalis. After a study of 44 cases of tabes dorsalis in which transurethral resection was performed at the Mayo Clinic, they feel that it is impossible to determine with any degree of accuracy in every case the proportion of vesical dysfunction caused by primary neurogenic atony and that produced by obstruction of the vesical neck. In most cases the tabetic condition was the predominating factor; in other cases it seemed definite that the predominating factor was obstruction at the vesical neck. It is entirely possible that in a few cases tabes dorsalis was only a coincidental finding and did not contribute to the vesical dysfunction. In the absence of an accurate method of distinguishing these conditions, it seems best to consider them as a single group.

Of the 44 patients, 43 were men and 1 was a woman. All except 4 were 50 or more years of age. Seventeen of the 44 patients complained of some type of "incontinence." In 6 cases the incontinence was nocturnal only, and in 1 case it was of a precipitate urgent type. In the remaining 10 cases the urinary leakage occurred during both day and night and varied in degree from the mild type consisting of an occasional involuntary spurt of urine to a more or less continual overflow type of dribbling from a distended bladder. In all except 1 case the bladder contained more than 200 cc. of residual urine; in 12 of the cases more than 300 cc. of residual urine was present. The largest amount found in any of these 17 cases was 1,200 cc.

Contractures of the vesical neck, small adenomatous collars and a small degree of hypertrophy of the lateral and median lobes predom-

68. Emmett, J. L., and Beare, J. B.: Transurethral Resection for Vesical Dysfunction in Cases of Tabes Dorsalis, J. A. M. A. **136**:1093 (April 24) 1948.

inated. It should be pointed out that in many cases cystoscopic examination revealed a relaxed and dilated vesical neck, which probably was not causing any obstruction. This appearance is due to the distended bladder, which has pulled open and stretched the vesical neck. In the majority of cases it was necessary to remove less than 10 Gm. of tissue; in only 9 cases was it necessary to remove more than 20 Gm.

The results of transurethral resection were most satisfactory and were classed as "good" in 39 cases and as "fair" in 3 cases. Two patients were unimproved. By the term "good," we mean that the patient is able to void with a good stream, can empty the bladder completely and does not have urinary incontinence. Of the 17 patients who complained of urinary incontinence prior to operation, 15 secured excellent results and complete relief of the incontinence.

Inasmuch as small degrees of obstruction of the vesical neck can precipitate vesical dysfunction in cases of tabes dorsalis, small degrees of postoperative contracture may conceivably cause a recurrence of the obstruction. Because of this, patients should be reexamined at yearly intervals to determine whether any residual urine is present. If it is, cystoscopic reexamination of the vesical neck should be performed and any scar tissue should be excised.

Carcinoma.—Mallah [69] reports on a patient having retention of urine of 500 cc. who was found on rectal palpation to have a prostate of medium size with irregularities of the right lobe which contained hard nodules, the infiltration extending to the right seminal vesicle. An implantation was made of 25 mg. of estradiol, and on the next day 4.5 Gm. of tissue was removed by endoscopic resection. Biopsy revealed epitheliomatous proliferation of characteristic acinotubular type. The patient was in poor general condition and, not being seen for some time, was believed to have died. After twenty months he was readmitted because of frequency of urination. The vesical residue at this time was 100 cc. Rectal palpation now revealed a flat prostate, with almost no irregularity of surface, which could hardly justify a diagnosis of carcinoma. No residual urine remained after three irrigations with a solution of silver nitrate. Roentgenologic examination of the spine and pelvis for metastatic lesions yielded negative results. The patient did not receive any oral treatment whatsoever. It has been suggested that in some cases it might be beneficial to combine oral therapy with implantation, as described by Gennes, and also that in some cases in which the disease is refractory implantation might replace oral administration. In the great majority of cases the oral route of administration is indicated.

69. Mallah, B.: Cancer de la prostate: Implantation de dihydrofolliculine: Résection et biopsie, J. d'urol. **54**:62 (Jan. 19) 1948.

After a review of the effect of estrogenic hormones on the prostate, and in particular on the mammary glands of the male, Reimann-Hunziker [70] describes in detail the case of a man of 68 years having cancer of the prostate treated by implantation of 100 mg. of ovocylin® (estradiol) on two occasions. The man did not have a familial history of cancer and had no other disease except an umbilical hernia. About a year after complaining of frequency, a diagnosis was made of carcinoma of the prostate. The tumor invaded the mucosa of the bladder. Since the condition was deemed inoperable, he was treated with implantation of 100 mg. of ovocylin.® His general condition improved, and the tumor in the vesical region disappeared. However, he was able to urinate spontaneously and suffered some transitory pain and swelling of the breasts, which gradually subsided. A few months later, a second implantation of 100 mg. of ovocylin® was made. The breasts became swollen and painful again, but this time there was no retrogression of the condition. The nipple of the left breast was inverted and a hard, almost immovable tumor the size of an egg was found as well as several pealike glands in the left axilla and left supraclavicular region. In the right breast was a walnut-sized tumor, with glandular swelling in the axilla and maxillary angle. Bilateral mastectomy was performed. Examination of the specimen showed adenocarcinoma. The patient died shortly thereafter of cachexia. Necropsy was not performed. A somewhat similar case was reported in the *Journal of Urology* in 1948, in which bilateral gynecomastia developed shortly before death after administration of 1,097 mg. of diethylstilbestrol for a period of four hundred and eighty-nine days.

Reports on reduction in the size of adenoma of the prostate after administration of synthetic estrogens vary, some showing this result in the majority of patients treated and others in as few as 15 per cent. Musiani's [71] experience was limited to 5 cases; he was able to demonstrate real reduction in only 1 of these. In this case reduction in size was only relative in spite of intramuscular injection of 485 mg. of hexestrol in ninety-seven days. The patient died of pyelonephritis. It is concluded that adenoma of the prostate may in certain cases be reduced by administration of estrogen owing to degeneration of the epithelium of the acini, which is replaced by connective tissue. This degeneration does not involve the whole adenoma and is limited to certain areas. In cancer of the prostate, favorable results have been reported in from 21 to 95 per cent of cases. Of the 10 patients with cancer in Musiani's series, 6 were benefited. Biopsy of an adenocarcinoma for which

70. Reimann-Hunziker, G.: Brustdrüsenkarzinom nach Ovocyclinbehandlung eines Prostatakarzinoms, Helvet. chir. acta. **15**:242 (July) 1948.

71. Musiani, U.: Action des oestrogènes de synthèse sur la prostate: Actions endocriniennes, J. d'urol. **54**:215, 1948.

estrogen therapy had not been used showed degeneration of the epithelial cells with nuclear pyknosis, but this was not so marked as in patients treated with estrogen.

Histologic section of a cancer which had been reduced in size by administration of 722 mg. of dienestrol for a period of one hundred and three days showed an appreciable reduction in the diameter of the nuclei, with rarefaction of chromatin. The protoplasmic membranes were partly torn or had disappeared, which indicated degeneration of the protoplasm. In the same section, however, were small islets of well preserved neoplastic cells. Masses of pyknotic nuclei were interspersed with fibrous connective tissue. Such findings may be observed also in untreated carcinoma. In 4 cases the author made a study of the pituitary gland. Three of the patients had received 105, 306 and 485 mg. of hexestrol and the other patient 722 mg. of dienestrol. The pituitary glands in these cases were a little heavier than normal (0.70 Gm.), and histologic section showed an increase in the percentage of principal cells, not unlike that seen during pregnancy. Gynecomastia is said to occur in 79 per cent of patients treated with estrogens. Cancer of the breast is a rare complication, but before treatment is begun care should be taken to exclude a familial disposition to cancer, and during and after treatment the condition of the breasts must be carefully observed. The author observed gynecomastia in 30 per cent of his patients treated with stilbestrol or hexestrol but none in the patients treated with dienestrol.

Guzman [72] is in agreement with Barringer that treatment of prostatic carcinoma with radiation will relieve dysuria and prolong life in comfort. He stated that the results compare favorably with those of transurethral resection, which were reported by Thompson and Emmett. They reported a 74 per cent incidence of one year survivals in a series of 253 cases, 46 per cent two year survivals, 31 per cent three year survivals, 17 per cent four year survivals and 8.7 per cent five year survivals. Before treatment is instituted for any patient having prostatic carcinoma, the method of choice for that patient should be determined, that is, transurethral resection, irradiation, castration with or without estrogens or some combination of these procedures. Irradiation is most useful in reducing the volume of the primary tumor and relieving pain due to metastasis. If the tumors arise in the periurethral glands, radiation can still be employed. Adequate testicular and regional irradiation diminishes the production of hormones. In this instance regional irradiation refers to irradiation to the lumboaortic and suprarenal regions. Irradiation should be given not only to the testes and the pelvis, but to the adrenal glands and the hypophysis to eliminate all extragonadal sources of androgen. In the past ten years Guzman has treated 25

72. Guzman, L.: Cancer of the Prostate, Radiology **49**:214 (Aug.) 1947.

patients for carcinoma of the prostate with radiation. In each instance there was pronounced diuresis but prompt relief of dysuria if adequate dosage could be given.

Buchert, Culp and Jones [73] reviewed 135 cases of carcinoma of the prostate, with complete follow-up examination in 134 cases. Seventy-nine patients had died; 55 were alive, and 1 could not be traced. Thirteen per cent of the patients treated for prostatism had carcinoma, of whom 30 per cent had demonstrable metastatic lesions when first seen. A correct diagnosis of carcinoma was made in 81 per cent by rectal examination. Carcinoma of the prostate is still a serious disease, and the prognosis is poor. Fifty per cent of the patients died during the first twelve months after presenting themselves for treatment. Radical perineal prostatectomy is the treatment of choice but is justified for 5 per cent or less of patients. For patients having retention of urine, transurethral resection followed by bilateral orchiectomy or estrogens or both seems to constitute the best treatment now available regardless of the presence or absence of demonstrable metastatic lesions. After complete resection of the obstructing tissue, ease and comfort in voiding with excellent control of the urine have been the rule. In 8 cases obstruction recurred and a second resection was required; 3 patients returned for a third resection. Of the 55 living patients, the health of 32 was classified as good, that of 16 fair and that of 7 poor. The condition of each patient has been followed for a minimum of nine months. Of the 79 patients who died, 13 died in the hospital after their primary admission. Three of these patients died after transurethral operation, 2 from bronchopneumonia and 1 from pulmonary embolism.

The application of the procedure of May and Stimmel [74] for the fractionation and photometric estimation of the urinary estrogens (estradiol, estrone and estriol) in a small series of cases with and without carcinoma of the prostate, after the administration of single therapeutic doses of the natural estrogens, reveals (1) that the difference is not consistent in the total excretion of estrogens, (2) that the presence or absence of the testes does not appear to alter the total excretion of estrogens or the relative distribution of estradiol, estrone and estriol in the urine and (3) that the patients with carcinoma of the prostate showed a tendency (75 per cent of 8 cases) to convert exogenous estrone into estriol more readily than did the patients without cancer, only 20 per cent

73. Buchert, W. I.; Culp, D. A., and Jones, G. H.: Carcinoma of the Prostate Gland: An Analysis of One Hundred and Thirty-Five Consecutive Cases, Pennsylvania M. J. **51**:165 (Nov.) 1947.

74. May, J. A., and Stimmel, B. F.: Do Patients with Cancer of the Prostate Gland Show Abnormal Metabolism of Therapeutic Doses of the Natural Estrogens? J. Urol. **59**:396 (March) 1948.

of whom (1 of 5 patients) behaved in this way. Lenninger and Scott reported that slices of prostate from human beings were incapable of metabolizing alpha-estradiol and estrone. This would seem to rule out the prostate as the agent of assault on the estrogenic molecule. The liver may be the important organ in the conversion of estrone to estriol.

Gutierrez [75] considers that the most important contribution of hormonal therapy to urology is that part which it plays in extending the indications for radical perineal prostatectomy, the only curative therapy for cancer of the prostate. With the judicious application of hormonal therapy, he foresees an increase in the number of cases amenable to operation from the former 10 per cent to nearly 80 per cent. The results of transurethral resection and of orchiectomy or hormonal therapy per se are merely palliative and offer the patient only transient relief from pain and obstruction and at most a somewhat prolonged survival. Hormonal therapy, and to a lesser extent orchiectomy, prior to radical operation will reduce the size of the gland, soften its stony consistency and frequently even cause regression in the malignant tumor itself, with reduction in the number of metastatic processes and sometimes their complete disappearance. In fact, Gutierrez describes 1 case of histologically demonstrable cancer of the prostate in which hormonal therapy was administered. Death resulted from intercurrent disease. Necropsy did not reveal any trace of malignant disease whatsoever, either in the prostate or in the lungs, which had earlier shown roentgenographic evidence of metastasis. This is an isolated case and does not imply a curative effect of hormonal therapy, which, in most cases, is followed by relapse or recurrence of the malignant process.

In another case transurethral resection for obstruction did not reveal any trace of cancer. However, three further transurethral resections were done elsewhere to relieve recurring obstruction, and the patient, who had refused to have orchiectomy, died of metastasis. In this case the primary malignant focus was located in the posterior lobe of the prostate, which is not accessible by transurethral resection. Even before the advent of hormonal therapy, radical perineal prostatectomy yielded cure in 50 per cent of the cases, and with the large increase of patients amenable to this treatment after administration of stilbestrol, it is hoped that there will be a trend toward more frequent use of this operation. The desired metamorphosis of the carcinoma can be accomplished by administration of stilbestrol (½ grain [0.032 Gm.] three times daily for the first month and 1 grain [0.065 Gm.] three times daily during the second month) for a short period previous to operation. Undesirable side effects are minimal with these small doses.

75. Gutierrez, R.: Metamorphosis of Cancer of the Prostate, Am. J. Surg. **74**:383 (Oct.) 1947.

According to the various degrees of involvement, three possible technics of operation are described, including (1) removal of the prostate with its capsule, followed by anastomosis of the membranous urethra to the vesical orifice in cases in which the tumor is limited to the prostate; (2) total prostatoseminal vesiculectomy with the same type of anastomosis, for cases of involvement of the prostate and seminal vesicles, and (3) the more radical procedure of Young, with removal of the prostate, seminal vesicles and vesical neck, for cases with involvement of these structures, followed by anastomosis of the membranous urethra to the remaining portion of the bladder. It is suggested that in the future stilbestrol might even be used prophylactically to prevent cancer of the prostate and thus reduce the incidence of this dread disease.

The incidence of prostatic carcinoma in the urologic department of St. Vincent's Hospital, Erie, Pa., as reported by McCaffery and Hess [76] for a six year period was 17.9 per cent of 1,100 cases of prostatic hypertrophy, or 197 cases. The highest incidence was noted in the group of patients 60 to 80 years of age, and the incidence was about equal in the groups 50 to 60 years and 80 to 90 years of age. The youngest patient was 47 years. None of the patients was referred to the urologist before the advent of irritative or obstructive symptoms. Nonurologic symptoms such as pain in the back and loss of weight may be present when metastasis to bone and lung has already developed. In 53 of the 197 cases roentgenograms showed evidence of metastatic processes, usually in the spine and pelvis. Correlation with the serum acid phosphatase level proved confusing. Changes of the skull in Paget's disease are especially helpful in making the differential diagnosis, since the serum acid phosphatase is frequently increased also in this disease. Orchiectomy was done in 141 patients; most of the other patients refused the operation. The importance of preoperative psychologic evaluation of each patient is stressed, since some men would rather die than lose their normal sexual function. The palliative results of the operation on the prostate, namely, relief of pain, gain in weight, removal of obstruction and prolongation of survival, were listed as 4 plus in 39 cases, 3 plus in 65 cases, 2 plus in 25 cases and 1 plus in 13 cases. Twenty-five patients, or 17.7 per cent, died in the hospital. Twenty-one did not show any improvement. All were seen too late to justify radical perineal operation.

If the patients could have been seen before the onset of symptoms, they might still have been amenable to curative perineal prostatectomy. Two other procedures of promise are preoperative administration of stilbestrol and orchiectomy, to be followed by radical operation when

76. McCaffery, R., and Hess, E.: The Treatment of Prostatic Carcinoma, J. Internat. Coll. Surgeons **11**:68 (Jan.-Feb.) 1948.

regression of the tumor has been demonstrated. Best results are obtained in adenocarcinoma since the more undifferentiated tumors do not respond to orchiectomy or treatment with stilbestrol.

FILARIASIS

Beach [77] states that early filariasis is manifested by recurrent attacks of lymphangitis associated with adenopathy, at times regional but more often generalized. The onset is usually abrupt and characterized by a transient red or livid streak in the superficial tissues of the upper part of the arm, the forearm or the leg. This streak follows the course of the subjacent lymphatic vessel. At times temporary swelling is present in the affected limb, most noticeable in the arm, and is accompanied with soreness and deep-seated aching. Regional glands may be enlarged, palpable and tender. Great prostration, elevation of temperature and leukocytosis do not occur, but most patients have slight eosinophilia. Of the 160 men examined, 37 showed implication of the genital organs. Acute vasitis or funiculitis was the commonest complication, being unilateral in 16 and bilateral in 3 instances. It began suddenly with pain and tenderness in the structures near the internal ring and in a matter of hours had rapidly descended through the inguinal canal and into the scrotum. The vas deferens seemed twice the usual size because of symmetric swelling of the tissues, and it soon became exquisitely tender to palpation. Acute vasitis manifested in early filariasis must be distinguished from subacute appendicitis; incomplete and indirect inguinal hernia, especially when the omentum is included; hydrocele of the cord; varicocele; torsion of the testicle, and subacute epididymitis. The blood picture is of diagnostic importance, as are the history and the objective findings. At present, the best treatment is early removal from the area where the disease is endemic. None of the many drugs used has proved completely satisfactory. According to Culbertson and Rose, the pentavalent, antimonial neostibosan® (ethylstibamine), is most satisfactory and promising. While this drug is well tolerated and efficient, its action on filariae is relatively slow.

CYSTINURIA

Yeh, Frankl, Dunn, Parker, Hughes and György [78] compared the daily excretions of fifteen amino acids by 7 normal females with those of a cystinuric girl 5 years of age for a period of five days. The normal excretion of arginine, cystine and lysine of the cystinuric patient

77. Beach, E. W.: Genital Manifestations in Early Filariasis, J. Urol. **59**:371 (March) 1948.

78. Yeh, H. L.; Frankl, W.; Dunn, M. S.; Parker, P.; Hughes, B., and György, P.: The Urinary Excretion of Amino Acids by a Cystinuric Subject, Am. J. M. Sc. **214**:507 (Nov.) 1947.

was increased markedly and that of glycine and histidine was notably decreased. This study confirms the work of other investigators, who have found that cystinuria is accompanied with a general disturbance in the metabolism of the amino acids.

REITER'S SYNDROME

Epstein [79] compares Reiter's disease with keratosis blennorrhagica and psoriasis arthropathica. The former disease seldom presents symptoms which suggest keratosis blennorrhagica, but when it does differentiation must be based on laboratory observations and the course of the disease. One feature of importance is that Reiter's disease does not lead to permanent changes in the joints, while ankylosis commonly supervenes in gonorrhea. The most important distinguishing features of Reiter's syndrome and psoriasis arthropathica are sex, initial manifestations, location of eruption and type of arthritis. Epstein reports an atypical case of Reiter's disease in which the patient responded favorably to fever therapy and transfusions after penicillin and sulfonamide compounds had been of little value.

URINARY INFECTION

Rohrer [80] states that the most important factor in the treatment of infections of the urinary tract is control of diabetes. Foci of infections, such as cutaneous lesions, boils, carbuncles and pyodermas, should be treated carefully and eliminated, if possible. Infected teeth and osteomyelitis and other infections should not be neglected. Operation and treatment should not be postponed because of diabetes. Care should be instituted to increase the patient's resistance, and his habits and activities should be so regulated that the highest physical welfare can be obtained. Anemia, constipation and irregular eating and sleeping habits should be corrected. In cases of gross pyuria hospitalization of the patient is of paramount importance. Frequent irrigation with a mild antiseptic solution by means of an inlying catheter and continuous drainage by catheter have cleared gross pyuria rapidly, especially in infections of the lower urinary tract. During the past twenty-five years, 2,674 diabetic patients have been examined at the Mason Clinic. Pyuria was about twice as common in the diabetic patient as in the nondiabetic person. Pyuria, because of lack of urinary symptoms in the diabetic patient, is frequently overlooked by the clinician. Resistance to treatment, recurrence and chronicity are common in the diabetic patient with infection of the urinary tract. Acute infections of the urinary tract,

79. Epstein, E.: Reiter's Disease; Comparison with Keratosis Blennorrhagica and with Psoriasis Arthropathica, Arch. Dermat. & Syph. **56**:191 (Aug.) 1947.

80. Rohrer, P. A.: Pyuria in the Diabetic, J. Urol. **59**:385 (March) 1948.

especially acute pyelitis, immediately raise the blood sugar level and increase insulin requirements. The importance of complete examination of the urinary tract in diabetic patients when urinalysis of a clean or catheterized specimen shows more than 10 pus cells to the field is stressed. A diabetic patient whose disease is properly controlled is not any greater risk for operation on the urinary tract than is the non-diabetic person.

Diehl and Hundley,[81] in discussing changes of the urinary tract in the presence of cervical carcinoma, state that the more advanced the original cervical carcinoma the more frequent is the association of dilatation of the urinary tract before the initiation of radiation therapy. The development of hydronephrosis and hydroureter during or after treatment has been associated with advancing malignant disease in every case and has invariably proved to be a grave prognostic sign. The urinary tract of the majority of patients with carcinoma, grades 1 and 2, did not show changes before therapy, and dilatation did not develop in any of the patients in these groups during the period of time between examinations. Urologic studies of all patients who have cervical carcinoma are indispensable for purposes of intelligent evaluation and management. Radiation therapy will not cause stricture of the ureter if the dosage is not excessive and provided the source of the ray is displaced from the ureter by accurate maximal vaginal packing.

TREATMENT

Sulfonamide Drugs.—Lehr[82] treated 700 unselected patients having systemic infections with a mixture containing equal amounts of sulfathiazole and sulfadiazine or sulfadiazine and sulfamerazine. Therapeutically effective concentrations were maintained in the blood with ease. Crystalluria was infrequent and never of the massive type observed so commonly during therapy with single compounds. In no case did any signs of renal irritation develop. Allergic reactions seemed to be decreased, and nausea and vomiting were rare. The results of these studies, which have been confirmed by other investigators, indicate that combinations of two or more sulfonamide compounds should be used in preference to single compounds for all indications, since they combine a high therapeutic efficacy with a remarkably low renal toxicity. Of more than 900 acid morning specimens which contained sulfonamide mixtures only 7 per cent were found to have moderate

81. Diehl, W. K., and Hundley, J. M., Jr.: Urinary Tract Changes in Cervical Carcinoma, Surg., Gynec. & Obst. **87**:705 (Dec.) 1948.

82. Lehr, D.: Prevention of Renal Damage by Use of Mixtures of Sulphonamides; Animal-Experimental and Clinical Studies, Brit. M. J. **2**:943 (Dec. 13) 1947.

or small amounts of sulfonamide crystals as contrasted with 29 per cent when sulfadiazine was used, 26 per cent with sulfamerazine and 70 per cent with sulfathiazole alone.

Berglin [83] discusses renal complications due to treatment with sulfonamide drugs and reports that under certain conditions concrements formed in relation to treatment with sulfonamide drugs are opaque to roentgen rays. He emphasizes the necessity of subjecting every patient to roentgenologic examination, since in certain cases this will settle the question of whether or not to resort to operation.

Penicillin.—Du Coudray [84] calls attention to the prevalence of symptomless subacute and chronic prostatitis discovered in the tropics after routine treatment of acute gonorrhea with penicillin (or the sulfonamide compounds), in doses generally accepted as adequate. Six cases are chosen to illustrate the main features of the condition and to prove that it can and does originate early in the course of acute primary gonorrhea, as it appears sometimes before and sometimes soon after apparently successful treatment with penicillin. Clinical evidence seems to indicate that prostatitis is a true infection due to invasion of the gland by gonococci or other organisms, or both. If that conclusion is correct, the following questions suggest themselves: 1. Why does the posterior urethra become infected simultaneously with the anterior urethra? 2. Why should a few gonococci survive the general and rapid destruction of the prostate, leaving the anterior urethra without evidence of infection? 3. Why are gonococci so difficult to recover from the prostate in cases of this kind? The type of prostatitis encountered is described in detail, and its cause is discussed although a theory of its causation is not advanced. Further careful and comprehensive investigations, with the use of controls, will have to be undertaken before the problem is finally solved and a more rapid and efficient form of treatment of the condition evolved.

Loewe and his co-authors [85] state that a new, dehydrated penicillin and gelatin–dextrose mixture taken in a single dose is effective for the routine treatment of acute, uncomplicated gonococcic urethritis. It is water soluble, nontoxic, nonirritant, nonallergenic and easy to administer by intramuscular or subcutaneous injection. Of the 128 patients suitable for statistical study, 123 (96.1 per cent) were satis-

83. Berglin, T.: Njurskadan vid sulfaterapi och frågan om sulfakonkrementens röntgentäthet, Nord. med. **34**:1355 (June 13) 1947.

84. Du Coudray, F. C. B.: Residual Subacute and Chronic Prostatitis after Penicillin and Sulfonamide Therapy in Acute Gonorrhoea, Brit. M. J. **2**:651 (Oct. 25) 1947.

85. Loewe, L.; Rosenthal, T.; Leifer, W.; Katzen, P.; Eiber, H. B., and Cohen, S.: Treatment of Acute Uncomplicated Gonococcal Urethritis with a Single Dose Water-Soluble Penicillin Preparation, J. Urol. **60**:958 (Dec.) 1948.

factorily "cured" and 2 (1.5 per cent) were probably reinfected. This result compares favorably with any previously reported series conducted in a similar manner.

Streptomycin.—Lattimer and his associates [86] give their experience with streptomycin in the treatment of genitourinary tuberculosis. Experiments were made in which a dosage of 1.8 mg. daily for one hundred and twenty days was used; this dose, however, proved to be toxic. Development of resistance to streptomycin limited its usefulness in some cases. The urine in most cases of tuberculosis of the kidney and in some cases of advanced lesions has stayed free from tubercle bacilli. Unilateral renal lesions, which pyelograms showed to be typical, failed to respond in 50 per cent of the cases. At present, Lattimer and his co-workers consider that such patients should undergo nephrectomy followed by treatment with streptomycin for three weeks and six months of care in a sanatorium. Prostatic nodules were not affected appreciably. Streptomycin did not cause swelling and tenderness to recede with increased rapidity in cases of epididymitis. All postoperative draining sinuses of the scrotum responded readily. Since the response to treatment with streptomycin in cases of epididymitis was so poor, operation, when indicated, is now used for cases in which only the genital organs are involved.

Testosterone.—Sheldon, Varden and Mark [87] divided 74 premature infants of both sexes into 3 groups: one a control group; one given methyl testosterone, 5 mg. daily, and one given testosterone propionate, 4 mg. daily. A distinct shortening in the time required to regain weight at birth and to gain 2,500 Gm. was noted in both groups which received the testosterone compounds. Four sets of twins were included in the study, and in each instance the one receiving the testosterone showed better somatic development than its control sibling. Sheldon, Varden and Mark do not advocate routine use of the testosterone compounds for premature infants but suggest such a procedure as an adjunct in the care of a selected group needing metabolic stimulation.

BIOPSY IN UROLOGIC PRACTICE

Kittredge [88] discusses the use of biopsy in urologic practice. In cases of tumors of the bladder the specimen is taken by means of

86. Lattimer, J. K.; Stearns, W. H.; Amberson, J. B.; Schwartz, J.; Goodman, R., and East, W.: The Streptomycin Treatment of Genito-Urinary Tuberculosis: A Preliminary Report, J. Urol. **60**:974 (Dec.) 1948.

87. Sheldon, E. K.; Varden, A. E., and Mark, J. S.: Experimental Use of Testosterone Compounds in Premature Infants, J. Clin. Endocrinol. **7**:708 (Oct.) 1947.

88. Kittredge, W. E.: The Use of Biopsy in Urologic Practice, Selected Writings by Staff Members of Ochsner Clinic **7**:16-17 (Dec. 31) 1948.

flexible forceps passed through the cytoscope or else by means of the resectoscope. All specimens are submitted for histologic study and graded. Carcinoma of the urethra is a fairly common condition, especially in women. Specimens for biopsy are removed by operative procedures. Carcinoma of the penis is responsible for 2 per cent of the malignant diseases that occur in males. It is limited almost exclusively to uncircumcised persons. The lesion usually begins in the coronal sulcus and is hidden by the prepuce. Specimens should be taken from the surface of these lesions, and biopsy should always be done to rule out malignant disease in cases of chronic, sloughing or proliferative penile sores. Carcinoma of the testis usually occurs in men less than 40 years of age, and a specimen for biopsy should be taken after surgical exposure of the testis. This specimen should be examined at once, and if the lesion is malignant, orchiectomy with high ligation should be carried out.

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